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NEWS 13 Nov 18 DKILIT has been renamed APOLLIT
NEWS 14 Nov 25 More calculated properties added to REGISTRY
NEWS 15 Dec 04 CSA files on STN
NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17 Dec 17 TOXCENTER enhanced with additional content
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
                ENERGY, INSPEC
NEWS 20 Feb 13 CANCERLIT is no longer being updated
NEWS 21 Feb 24 METADEX enhancements
NEWS 22 Feb 24 PCTGEN now available on STN
NEWS 23 Feb 24 TEMA now available on STN
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25 Feb 26 PCTFULL now contains images
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        Mar 20
                EVENTLINE will be removed from STN
NEWS 28
        Mar 24
                PATDPAFULL now available on STN
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        Mar 24
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                structures available in REGISTRY
        Apr 11
                Display formats in DGENE enhanced
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NEWS 31
        Apr 14
                MEDLINE Reload
                Polymer searching in REGISTRY enhanced
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        Apr 17
                Indexing from 1947 to 1956 added to records in CA/CAPLUS
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        Jun 13
NEWS 34
        Apr 21
                New current-awareness alert (SDI) frequency in
                WPIDS/WPINDEX/WPIX
NEWS 35
        Apr 28
                RDISCLOSURE now available on STN
NEWS 36
        May 05
                Pharmacokinetic information and systematic chemical names
                added to PHAR
NEWS 37
        May 15
                MEDLINE file segment of TOXCENTER reloaded
                Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 38
        May 15
```

STN search for 09/256,156 26/06/2003 NEWS 39 May 16 CHEMREACT will be removed from STN NEWS 40 Simultaneous left and right truncation added to WSCA May 19 NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB NEWS 43 Jun 06 PASCAL enhanced with additional data NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available NEWS 45 Jun 25 HSDB has been reloaded NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003 NEWS HOURS STN Operating Hours Plus Help Desk Availability NEWS INTER General Internet Information NEWS LOGIN Welcome Banner and News Items NEWS PHONE Direct Dial and Telecommunication Network Access to STN NEWS WWW CAS World Wide Web Site (general information) Enter NEWS followed by the item number or name to see news on that specific topic. All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may

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=> s IqG3 13221 IGG3

=> s constant(1w)region or CH2(1w)domain 19122 CONSTANT(1W) REGION OR CH2(1W) DOMAIN

=> s 11 and 12

L33480 L1 AND L2

=> dup rem 13

PROCESSING IS APPROXIMATELY 43% COMPLETE FOR L3 PROCESSING IS APPROXIMATELY 85% COMPLETE FOR L3

PROCESSING COMPLETED FOR L3

3378 DUP REM L3 (102 DUPLICATES REMOVED)

=> s 14 not py>=1999

4 FILES SEARCHED...

486 L4 NOT PY>=1999

=> s 15 and (mutat? or delet? or substitut?)

380 L5 AND (MUTAT? OR DELET? OR SUBSTITUT?)

=> s 16 not py>=1998

287 L6 NOT PY>=1998

=> s 17 and ((reduc? or decreas? or less?)(3w)(bind? or affinity))

4 FILES SEARCHED...

80 L7 AND ((REDUC? OR DECREAS? OR LESS?)(3W)(BIND? OR AFFINITY)) R,T

=> s 18 and Fc receptor

21 L8 AND FC RECEPTOR

=> d ibib abs 1-21

ANSWER 1 OF 21 USPATFULL

ACCESSION NUMBER:

97:61594 USPATFULL

TITLE:

DNA encoding antibodies with altered effector functions

INVENTOR(S): Winter, Gregory Paul, Cambridge, Great Britain

Duncan, Alexander Robert, Wimbledon, United Kingdom Burton, Dennis Raymond, Sheffield, Great Britain

Scotgen Biopharmaceuticals Incorporated, Menlo Park, PATENT ASSIGNEE(S):

CA, United States (U.S. corporation)

NUMBER KIND DATE ______ US 5648260 PATENT INFORMATION: 19970715 US 1995-478825 19950607 (8)

APPLICATION INFO.: RELATED APPLN. INFO.:

Continuation of Ser. No. US 1994-208084, filed on 9 Mar

1994 which is a continuation of Ser. No. US

1991-814035, filed on 24 Dec 1991, now abandoned which is a continuation of Ser. No. US 1989-303668, filed on

18 Jan 1989, now abandoned

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1987-6425 GB 1987-18897 GB 1987-28042 WO 1988-GB211	19870318 19870810 19871201 19880318
DOCUMENT TYPE: FILE SEGMENT: PRIMARY EXAMINER: ASSISTANT EXAMINER: LEGAL REPRESENTATIVE: NUMBER OF CLAIMS: EXEMPLARY CLAIM:	Utility Granted Feisee, Lila Reeves, Julie E. Spencer & Frank 30	

NUMBER OF DRAWINGS: 11 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 845

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The DNA encoding an antibody with an altered function, e.g. altered

affinity for an effector ligand such as Fc receptor

(FcR) on a cell or the Cl component of complement is produced by replacing the nucleic acid encoding at least one amino acid residue in the constant portion of the antibody with nucleic acid encoding a

different residue.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 2 OF 21 USPATFULL

ACCESSION NUMBER: 97:49532 USPATFULL

TITLE:

Expression vectors encoding bispecific fusion proteins

and methods of producing biologically active bispecific

fusion proteins in a mammalian cell

INVENTOR(S): Ledbetter, Jeffrey A., Seattle, WA, United States

Gilliland, Lisa K., Seattle, WA, United States Hayden, Martha S., San Diego, CA, United States Linsley, Peter S., Seattle, WA, United States Bajorath, Jurgen, Everett, WA, United States Fell, H. Perry, Redmond, WA, United States

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, New York, NY, United

States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5637481 19970610 US 1993-121054 APPLICATION INFO.: 19930913 (8)

Continuation-in-part of Ser. No. US 1993-13420, filed RELATED APPLN. INFO.:

on 1 Feb 1993, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Guzo, David

LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell Welter & Schmidt

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM:

23 Drawing Figure(s); 17 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 2109

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides an expression vector encoding monospecific or bispecific fusion protein. In one embodiment the expression vector encodes a monospecific fusion protein, which vector comprises a recombinant monospecific single chain cassette comprising a DNA sequence encoding a first binding domain capable of binding a cell surface antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9ANSWER 3 OF 21 USPATFULL

ACCESSION NUMBER: 97:36082 USPATFULL

TITLE: Antibodies with altered effector functions INVENTOR(S): Winter, Gregory P., Cambridge, Great Britain Duncan, Alexander R., Wimbledon, Great Britain

Burton, Dennis R., Sheffield, Great Britain

PATENT ASSIGNEE(S): Scotgen Biopharmaceuticals Incorporated, Menlo Park,

CA, United States (U.S. corporation)

1994 which is a continuation of Ser. No. US 1991-814035, filed on 24 Dec 1991, now abandoned which is a continuation of Ser. No. US 1989-303668, filed on

18 Jan 1989, now abandoned

FILE SEGMENT: Granted
PRIMARY EXAMINER: Feisee, Lia
ASSISTANT EXAMINER: Reeves, Julie E.
LEGAL REPRESENTATIVE: Spencer & Frank

NUMBER OF CLAIMS: 25 EXEMPLARY CLAIM: 14

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 864

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An antibody with an altered function, e.g. altered affinity for an effector ligand such as **Fc receptor** (FcR) on a cell

or the C1 component of complement is produced by replacing at least one amino acid residue in the constant portion of the antibody with a

different residue.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 4 OF 21 USPATFULL

ACCESSION NUMBER: 96:116108 USPATFULL

TITLE: Humanized anti-CD3 specific antibodies
INVENTOR(S): Bolt, Sarah L., Cambridge, England
Clark, Michael R., Cambridge, England
Gorman, Scott D., Great Shelford, England

Gorman, Scott D., Great Shelford, England
Routledge, Edward G., Great Shelford, England
Waldmann, Horman, Cambridge, England

Waldmann, Herman, Cambridge, England

PATENT ASSIGNEE(S): British Technology Group Limited, London, England

(non-U.S. corporation)

19930309 PCT 371 date 19930309 PCT 102(e) date

NUMBER DATE

PRIORITY INFORMATION: GB 1992-6422 19920324

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Eisenschenk, Frank C. LEGAL REPRESENTATIVE: Nixon & Vanderhye

NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 1008

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel aglycosylated antibodies having a binding affinity for the CD3 antiqen complex are of value for use in therapy, particularly in

immunosuppression.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 21 PCTFULL COPYRIGHT 2003 Univentio

**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L9 ANSWER 6 OF 21 PCTFULL COPYRIGHT 2003 Univentio

**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER
**** DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L9 ANSWER 7 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1997044362 PCTFULL ED 20020514

TITLE (ENGLISH): MUTATED NONACTIVATING IGG2 DOMAINS AND

ANTI-CD3 ANTIBODIES INCORPORATING THE SAME

TITLE (FRENCH): DOMAINES D'IGG2 MUTANTS ET NON ACTIVANTS ET ANTICORPS

ANTI-CD3 LES COMPRENANT

INVENTOR(S): TSO, J., Yun;

COLE, Michael, S.; ANASETTI, Claudio

PATENT ASSIGNEE(S): PROTEIN DESIGN LABS, INC.;

FRED HUTCHINSON CANCER RESEARCH CENTER;

TSO, J., Yun; COLE, Michael, S.; ANASETTI, Claudio

LANGUAGE OF PUBL: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE
----WO 9744362 A1 19971127

DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE

ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE

SN TD TG

APPLICATION INFO.: WO 1997-US8576 A 19970519 PRIORITY INFO.: US 1996-8/650,410 19960520 US 1996-8/656,586 19960531

ABEN The invention provides mutated IgG2 constant regions and

anti-CD3 antibodies incorporating the

same. Such antibodies specifically bind to the CD3 antigen on T-cells but induce reduced mitogenic

response compared with otherwise identical antibodies bearing natural IqG2 constant regions. The

antibodies can be used for treating disorders requiring immune

suppression with fewer side effects

than result from treatment with prior anti-CD3 antibodies.

ABFR L'invention concerne des regions constantes d'IgG2 mutantes et des anticorps anti-CD3 les

comprenant. Lesdits anticorps se fixent specifiquement a l'antigene CD3 sur les lymphocytes T mais

induisent une reponse mitogenique reduite par rapport aux anticorps autrement identiques portant des

regions constantes d'IgG2 naturelles. Les dits anticorps peuvent etre utilises pour traiter les

troubles necessitant la suppression de la reaction immunitaire avec moins d'effets secondaires

qu'avec les traitements anterieurs au moyen desdits anticorps anti-CD3 sus-mentionnes.

L9 ANSWER 8 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1997034631 PCTFULL ED 20020514

TITLE (ENGLISH): IMMUNOGLOBIN-LIKE DOMAINS WITH INCREASED HALF LIVES TITLE (FRENCH): DOMAINES ANALOGUES A L'IMMUNOGLOBULINE A DEMI-VIES

PROLONGEES

INVENTOR(S): WARD, Elizabeth, Sally

PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM;

WARD, Elizabeth, Sally

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KG KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US3321 A 19970303 PRIORITY INFO.: US 1996-60/013,563 19960318

ABEN Disclosed are recombinant vectors encoding immunoglobulin-like domains and portions thereof,

such as antibody Fc-hinge fragments, subfragments and mutant domains with extended biological half

lives. Methods of producing large quantities of such domains,

heterodimers, and fusion proteins

following expression by host cells are also reported. Described are antibody Fc and Fc-hinge

domains, which have the same in vivo stability as intact antibodies; and domains engineered to have

increased in vivo half lives. These DNA constructs and protein domains will be useful as templates $% \left(1\right) =\left(1\right) +\left(1\right)$

for in vitro mutagenesis and high resolution structural studies; for immunization and vaccination;

and for the production of recombinant antibodies or chimeric proteins with increased stability and

longevity for therapeutic and diagnostic uses.

ABFR Vecteurs recombinants codant des domaines analogues a l'immunoglobuline et des parties de ces

derniers, tels que des domaines mutants, des sous-fragments et des

fragments de Fc-charniere (Fc-hinge) anticorpaux, a demi-vies biologiques prolongees. Des procedes de production en grandes quantites de tels domaines, heterodimeres et proteines fusionnees apres leur expression par des cellules hotes sont egalement decrits, ainsi que des domaines Fc et Fc-charniere anticorpaux, qui presentent la meme stabilite in vivo que les anticorps intacts; et des domaines genetiquement modifies de facon a presenter des demi-vies in vivo prolongees. Ces ADN de recombinaison et ces domaines proteiques seront utiles comme matrices pour la mutagenese in vitro et pour les etudes de structures de haute resolution; pour l'immunisation et la vaccination; ainsi que pour la production d'anticorps recombinants ou de proteines chimeriques a stabilite et longevite accrue destines a des usages therapeutiques et diagnostiques.

PCTFULL COPYRIGHT 2003 Univentio ANSWER 9 OF 21 L9 1997030089 PCTFULL ED 20020514 ACCESSION NUMBER: NOVEL ANTIBODY-CYTOKINE FUSION PROTEIN, AND METHODS OF TITLE (ENGLISH): MAKING AND USING THE SAME TITLE (FRENCH): NOUVELLE PROTEINE DE FUSION ANTICORPS-CYTOKINE ET METHODES D'ELABORATION ET D'UTILISATION DE CETTE PROTEINE INVENTOR(S): HARVILL, Eric, T.; MORRISON, Sherie, L. PATENT ASSIGNEE(S): HARVILL, Eric, T.; MORRISON, Sherie, L. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE ______ WO 9730089 A1 19970821

DESIGNATED STATES

AU CA IL JP US AT BE CH DE DK ES FI FR GB GR IE IT LU

MC NL PT SE

APPLICATION INFO.: WO 1997-US1420 A 19970211 US 1996-60/011,569 PRIORITY INFO.: 19960213

By fusing a cytokine (e.g., IL-2) to an antibody (e.g. IgG3),

a molecule has been created with

the functional characteristics of both proteins. The pharmacokinetic properties of such a fusion

protein may be greatly improved over those of cytokine alone (e.g., IL-2) and previously described

antibody-IL-2 fusions. The molecule is intact and recoverable from the blood of mice hours after

intraperitoneal injection. The present fusion protein also reaches distant organs throughout the

animal. The 7-hour half-life in vivo of an exemplary IL2-IgG3 molecule is much longer than that of

IL-2 and may make it more useful than IL-2 for multiple in vivo applications. Other IL-2 fusion

proteins used as vaccines have been shown to elicit an increased immune response against the fused

protein and have been studied for both prevention and treatment against tumors and viruses

```
expressing those antigens. The exemplary IgG3-IL2 fusion
       protein binds a hapten that can be
       conjugated to most antigens of interest. Antigens can therefore be
       linked to bioactive IL-2 without
       the complexities and uncertainties of making IL-2 fusions with each
       antigen individually. This
       approach has been tested using BSA as a model antigen. The antibody
       response to IgG3-IL2-bound BSA
       is increased over that of BSA or IgG3-bound BSA. This system
       should be useful in potentiating the
       immune response to antigen and in screening antigens for use in
       vaccines.
       Par fusion d'une cytokine (par exemple IL-2) a un anticorps (par exemple
ABFR
       IqG3), on obtient une
       molecule presentant les caracteristiques fonctionnelles des deux
       proteines. Les caracteristiques
       pharmacocinetiques d'une telle proteine de fusion peuvent etre
       considerablement ameliorees par
       rapport a celles de la cytokine seule (telle IL-2) et les fusions
       anticorps-IL-2 precedemment
       decrites. La molecule est intacte; elle peut etre extraite du sang d'une
       souris quelques heures
       apres une injection intraperitoneale. La presente proteine de fusion
       atteint egalement des organes
       eloignes les uns des autres dans tout l'organisme de l'animal. La
       demi-vie de 7 heures in vivo d'une
       molecule IL-2 IgG3 typique est bien superieure a celle d'une
       molecule IL-2, ce qui peut la rendre
       plus utile qu'une molecule IL-2 pour de multiples applications in vivo.
       Il est apparu que d'autres
       proteines de fusion IL-2 utilisees comme vaccin declenchent une reponse
       immunitaire plus forte par
       rapport a la proteine fusionnee et ont ete etudiees pour la prevention
       et pour le traitement des
       tumeurs et des virus exprimant ces antigenes. La proteine de fusion
       typique IgG3-IL2 se lie a un
       haptene pouvant etre conjuge a la plupart des antigenes vises. Des
       antigenes peuvent donc etre lies
       a l'IL-2 bioactive sans les complexites et les incertitudes des fusions
       d'IL-2 avec chaque antiqene
       individuellement. Cette demarche a ete testee en utilisant la
       serum-albumine bovine (BSA) comme
       antiquee modele. La reponse des anticorps a cette BSA liee a
       IgG3-IL2 est plus forte que celle de la
       BSA, seule, ou liee a IgG3. Ce systeme devrait etre utile pour
       potentialiser la reponse immunitaire
       a l'antigene et selectionner les antigenes destines a des vaccins.
       ANSWER 10 OF 21
                        PCTFULL
                                   COPYRIGHT 2003 Univentio
ACCESSION NUMBER:
                        1997028267 PCTFULL ED 20020514
                        ANTIBODIES AND IMMUNOGLOBULIN FUSION PROTEINS HAVING
TITLE (ENGLISH):
                        MODIFIED EFFECTOR FUNCTIONS AND USES THEREFOR
TITLE (FRENCH):
                        ANTICORPS ET PROTEINES DE FUSION D'IMMUNOGLOBULINE
                        PRESENTANT DES FONCTIONS D'EFFECTEUR MODIFIEES ET LEURS
                        UTILISATIONS
INVENTOR(S):
                        GRAY, Gary, S.;
                        CARSON, Jerry;
                        JAVAHERIAN, Kashi;
                        JELLIS, Cindy, L.;
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STN search for 09/256,156 26/06/2003 RENNERT, Paul, D.; SILVER, Sandra PATENT ASSIGNEE(S): REPLIGEN CORPORATION; GRAY, Gary, S.; CARSON, Jerry; JAVAHERIAN, Kashi; JELLIS, Cindy, L.; RENNERT, Paul, D.; SILVER, Sandra LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 9728267 A1 19970807 DESIGNATED STATES AU CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC W: NL PT SE APPLICATION INFO.: WO 1997-US1698 A 19970203 US 1996-8/595,590 19960202 PRIORITY INFO.: CTLA4-immunoglobulin fusion proteins having modified immunoglobulin constant region-mediated effector functions, and nucleic acids encoding the fusion proteins, are described. The CTLA4-immunoglobulin fusion proteins comprise two components: a first peptide having a CTLA4 activity and a second peptide comprising an immunoglobulin constant region which is modified to reduce at least one constant region-mediated biological effector function relative to a CTLA4-IqG1 fusion protein. The nucleic acids of the invention can be integrated into various expression vectors, which in turn can direct the synthesis of the corresponding proteins in a variety of hosts, particularly eukaryotic cells. The CTLA4-immunoglobulin fusion proteins described herein can be administered to a subject to inhibit an interaction between a CTLA4 ligand (e.g., B7-1 and/or B7-2) on an antigen presenting cell and a receptor for the CTLA4 ligand (e.g., CD28 and/or CTLA4) on the surface of T cellsto thereby suppress an immune response in the subject, for example to inhibit transplantation rejection, graft versus host disease or autoimmune responses. ABFR Proteines de fusion de CTLA4-immunoglobuline presentant des fonctions d'effecteur par la region constante d'immunoglobuline modifiees, et acides nucleiques codant les proteines de fusion. Les proteines de fusion de CTLA4-immunoglobuline sont constituees de deux elements: un premier peptide presentant une activite CTLA4 et un deuxieme peptide comprenant une region constante d'immunoglobuline modifiee pour reduire au moins une fonction

constante d'immunoqlobuline, par rapport a une proteine de fusion

decrits peuvent s'integrer dans differents vecteurs d'expression,

commander la synthese des proteines correspondantes dans differents

lesquels peuvent a leur tour

d'effecteur biologique par la region

CTLA4-IgG1. Les acides nucleiques

hotes, en particulier les

cellules eucaryotes. Les proteines de fusion de CTLA4-immunoglobuline decrites ici peuvent etre

administrees a un sujet pour inhiber une interaction entre un ligand DTLA4 (par exemple, B7-1 et/ou

B7-2) sur une cellule presentant un antigene et un recepteur pour le ligand CTLA4 (par exemple CD28

et/ou CTLA4) a la surface de cellules T pour supprimer ainsi une reponse immunitaire du sujet, par

exemple pour inhiber le rejet de transplantation, les reaction de greffon contre l'hote ou les

reactions auto-immunes.

ANSWER 11 OF 21 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1997017446 PCTFULL ED 20020514

TITLE (ENGLISH): HUMANIZED ANTIBODIES TO HUMAN 9D39, COMPOSITIONS

CONTAINING AND THERAPEUTIC USE THEREOF

ANTICORPS HUMANISES DIRIGES CONTRE LA 9p39 D'ORIGINE TITLE (FRENCH):

HUMAINE, COMPOSITIONS CONTENANT CES ANTICORPS ET LEUR

UTILISATION THERAPEUTIQUE

BLACK, Amelia; INVENTOR(S):

HANNA, Nabil; PADLAN, Eduardo, A.; NEWMAN, Roland, A.

IDEC PHARMACEUTICAL CORPORATION PATENT ASSIGNEE(S):

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 9717446 A2 19970515

W:

AU CN FI HU JP KR NO NZ AT BE CH DE DK ES FI FR GB GR
IE IT LU MC NL PT SE

APPLICATION INFO.:

WO 1996-US17875

A 19961107

PRIORITY INFO.:

US 1995-8/554 840

The present invention is directed to humanized antibodies which bind ABEN

human qp39 and their use

as therapeutic agents. These humanized antibodies are especially useful for treatment of autoimmune

diseases.

ABFR La presente invention concerne des anticorps humanises se liant a la gp39 d'origine humaine

ainsi que leur utilisation comme agents therapeutiques. Ces anticorps humanises conviennent

particulierement au traitement des affections auto-immunes.

ANSWER 12 OF 21 PCTFULL COPYRIGHT 2003 Univentio T.9

1997003687 PCTFULL ED 20020514 ACCESSION NUMBER:

SOLUBLE LYMPHOTOXIN-'beta' RECEPTORS AND TITLE (ENGLISH):

> ANTI-LYMPHOTOXIN RECEPTOR AND LIGAND ANTIBODIES, AS THERAPEUTIC AGENTS FOR THE TREATMENT OF IMMUNOLOGICAL

DISEASE

TITLE (FRENCH): RECEPTEURS SOLUBLES DE LA LYMPHOTOXINE-'beta',

> RECEPTEUR ANTI-LYMPHOTOXINE ET ANTICORPS LIGANDS SERVANT D'AGENTS POUR LE TRAITEMENT DE TROUBLES

IMMUNOLOGIOUES

BROWNING, Jeffrey, L.; INVENTOR(S):

BENJAMIN, Christopher, D.;

HOCHMAN, Paula, S.

PATENT ASSIGNEE(S): BIOGEN, INC.; BROWNING, Jeffrey, L.; BENJAMIN, Christopher, D.; HOCHMAN, Paula, S. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 9703687 A1 19970206 DESIGNATED STATES AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES W : FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG A 19960719 APPLICATION INFO.: WO 1996-US12010 PRIORITY INFO.: US 1995-8/505,606 19950721 ABEN This invention relates to compositions and methods comprising lymphotoxin-'beta' receptor blocking agents, which block lymphotoxin-'beta' receptor signalling. Lymphotoxin-'beta' receptor blocking agents are useful for treating lymphocyte-mediated immunological diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses. This invention relates to soluble forms of the lymphotoxin-'beta' receptor extracellular domain that act as lymphotoxin-'beta' receptor blocking agents. This invention also relates to the use of antibodies directed against either the lymphotoxin-'beta' receptor or its ligand, surface lymphotoxin, that act as lymphotoxin-'beta' receptor blocking agents. A novel screening method for selecting soluble receptors, antibodies and other agents that block LT-'beta' receptor signalling is provided. ABFR L'invention porte sur des compositions et procedes relatifs a des agents de blocage du recepteur de la lymphotoxine-'beta' bloquant la signalisation dudit recepteur et qui s'averent utiles pour le traitement des troubles immunologiques induits par les lymphocytes, et plus particulierement pour inhiber les reponses immunitaires induites par les cellules Th1. L'invention, qui porte sur des formes solubles du domaine extracellulaire du recepteur de la lymphotoxine-'beta' servant d'agents de blocage du recepteur de la lymphotoxine-'beta', a egalement trait a l'utilisation d'anticorps agissant soit contre le recepteur de la lymphotoxine-'beta', soit contre ses ligands, et a des lymphotoxines de surface agissant comme agents de blocage du recepteur de la lymphotoxine-'beta'. L'invention porte par ailleurs sur une nouvelle methode de criblage permettant de selectionner les recepteurs solubles, les anticorps et autres agents bloquant la signalisation du recepteur LT-'beta'.

Ь9

ACCESSION NUMBER:

ANSWER 13 OF 21 PCTFULL

CHIMERIC LEPTIN FUSED TO IMMUNOGLOBULIN DOMAIN AND USE TITLE (ENGLISH): TITLE (FRENCH): LEPTINE CHIMIRASEE PAR FUSION AVEC UN DOMAINE D'IMMUNOGLOBULINE ET UTILISATION CORRESPONDANTE INVENTOR(S): BROWNE, Michael, Joseph; CHAPMAN, Conrad, Gerald; CLINKENBEARD, Helen, Elizabeth; ROBINSON, Jeffrey, Hugh PATENT ASSIGNEE(S): SMITHKLINE BEECHAM PLC; BROWNE, Michael, Joseph; CHAPMAN, Conrad, Gerald; CLINKENBEARD, Helen, Elizabeth; ROBINSON, Jeffrey, Hugh English LANGUAGE OF PUBL.: DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 9700319 A2 19970103 DESIGNATED STATES W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1996-GB1388 A 19960611 PRIORITY INFO.: GB 1995-9511935.0 19950613 ABEN Chimeric leptin which are proteins comprising leptin or a mutant or a variant thereof fused to a human immunogobulin domain. One favoured immunoglobulin domain is the human immunoglobulin Fc domain. The chimeric derivatives of leptin have, despite their large molecular size, good pharmacological activity combined with prolonged clearance rates. These derivatives of leptin are therefore indicated to be particularly useful for the treatment or prophylaxis of obesity or diseases and conditions associated with obesity such as atherosclerosis, hypertension and type II diabetes. ABFR La presente invention concerne de la leptine chimerisee, a savoir des proteines comprenant de la leptine, l'un de ses mutants, ou l'une de ses variantes, fusionnees a un domaine d'immunoglobuline humaine. L'un des domaines preferes d'immunoglobuline est le domaine Fc de l'immunoglobuline humaine. Malgre leur grande taille moleculaire, ces derives chimeriques de la leptine presentent une bonne activite pharmacologique combinee a des durees elevees d'elimination par l'organisme. Ces derives de leptine conviennent donc particulierement pour le traitement ou la prophylaxie de l'obesite ou des affections et etats associes a l'obesite tels que l'atherosclerose, l'hypertension et le diabete de type II.

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1997000319 PCTFULL ED 20020514

STN search for 09/256,156 26/06/2003 ANSWER 14 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1996006625 PCTFULL ED 20020514 TITLE (ENGLISH): ANTIBODY CONSTRUCTS WITH CDR SWITCHED VARIABLE REGIONS TITLE (FRENCH): ANTICORPS RECOMBINES COMPORTANT DES REGIONS VARIABLES PERMUTEES AVEC DES REGIONS DETERMINANT LA COMPLEMENTARITE (CDR) INVENTOR (S): ILL, Charles, R.; LUDWIG, James, Richard; RATHNACHALAM, Radhakrishnan ELI LILLY AND COMPANY; PATENT ASSIGNEE(S): ILL, Charles, R.; LUDWIG, James, Richard; RATHNACHALAM, Radhakrishnan LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE WO 9606625 A1 19960307 DESIGNATED STATES AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE W: HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1995-US10791 A 19950825 PRIORITY INFO.: US 1994-8/296,625 19940826 CDR grafted recombinant antibodies are provided which have at least one ABEN CDR switched variable domain wherein one or more of the heavy chain CDRs from one chain of the donor antibody are grafted into the framework regions of the light chain of the acceptor antibody. To enhance the binding of the CDRs as well as the secretion level of multi-chain constructs, the recombinant antibodies are altered using techniques of molecular modeling. L'invention concerne des anticorps recombines greffes avec des regions ABFR

determinant la

complementarite (CDR), presentant au moins un domaine variable permute avec des CDR, dans lequel au

moins une des CDR des chaines lourdes provenant d'une chaine de l'anticorps donneur est greffee dans

les regions d'infrastructure de la chaine legere de l'anticorps receveur. Afin de favoriser la

fixation des CDR et d'augmenter le niveau de secretion de produits de recombinaison a chaines

multiples, les anticorps recombines sont modifies au moyen de techniques de modelisation moleculaire.

ANSWER 15 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1996004388 PCTFULL ED 20020514

TITLE (ENGLISH): NOVEL COMPOUNDS TITLE (FRENCH): NOUVEAUX COMPOSES INVENTOR(S):

BROWNE, Michael, Joseph; MURPHY, Kay, Elizabeth; CHAPMAN, Conrad, Gerald;

CLINKENBEARD, Helen, Elizabeth;

YOUNG, Peter, Ronald;

SHATZMAN, Allan, Richard

SMITHKLINE BEECHAM PLC; PATENT ASSIGNEE(S):

SMITHKLINE BEECHAM CORPORATION;

BROWNE, Michael, Joseph; MURPHY, Kay, Elizabeth; CHAPMAN, Conrad, Gerald;

CLINKENBEARD, Helen, Elizabeth;

YOUNG, Peter, Ronald; SHATZMAN, Allan, Richard

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

NUMBER KIND DATE WO 9604388 A1 19960215

DESIGNATED STATES

AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE W :

HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 1995-EP3036 A 19950728 GB 1994-9415379.8 19940729 US 1995-8/468,297 19950606

ABEN A soluble protein having IL4 and/or IL13 antagonist or partial

antagonist activity comprises an

IL4 mutant or variant fused to at least one human immunoqlobulin

constant domain or fragment

ABFR Proteine soluble ayant une activite antagoniste complete ou partielle de IL4 (interleukine 4)

et/ou de IL13, qui comprend un variant ou mutant de IL4 fusionne avec au moins un domaine constant

d'immunoglobuline humaine ou fragment dudit domaine.

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1995009917 PCTFULL ED 20020514 ACCESSION NUMBER:

GENETICALLY ENGINEERED BISPECIFIC TETRAVALENT TITLE (ENGLISH):

ANTIBODIES

ANTICORPS BISPECIFIQUES ET TETRAVALENTS, OBTENUS PAR TITLE (FRENCH):

GENIE GENETIQUE

INVENTOR (S): MORRISON, Sherie, L.;

COLOMA, M., Josefina

PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE ______ WO 9509917 A1 19950413

DESIGNATED STATES

CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE W :

PRIORITY INFO.: WO 1994-US11411 A 19941007 US 1993-8/134,556 19931007

ABEN The invention relates to a method for the production of recombinant

bispecific tetravalent

antibodies. These antibodies are useful in targeting toxins and

activated T cells to tumor cells as

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a DNA segment encoding a
       single chain antibody with a DNA segment encoding an IgG
       constant region. This fusion is then
       ligated to a DNA segment encoding a heavy chain variable region with
       different specificity. Cells
       are cotransfected with this construct and a vector encoding a light
       chain variable region having the
       same specificity as the heavy chain variable region.
ABFR
      L'invention concerne un procede de preparation d'anticorps de
       recombinaison bispecifiques et
       tetravalents. Ces anticorps sont utiles pour cibler des toxines et des
       cellules T activees sur des
       cellules tumorales ainsi que pour des diagnostics immunologiques. On
       prepare ces anticorps en
       fusionnant un segment d'ADN codant pour un anticorps a chaine unique
       avec un segment d'ADN codant
       pour une region constante d'IgG. Ce produit de fusion est ensuite lie a
       un segment d'ADN codant pour
       une region variable des chaines lourdes, presentant une specificite
       differente. On realise une
       transfection simultanee de cellules avec cette structure de
       recombinaison et un vecteur codant pour
       une region variable des chaines legeres, ayant la meme specificite que
       la region variable des
       chaines lourdes.
      ANSWER 17 OF 21 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1994029351 PCTFULL ED 20020513
TITLE (ENGLISH):
                       ANTIBODIES
TITLE (FRENCH):
                       ANTICORPS
INVENTOR(S):
                       MORGAN, Susan, Adrienne;
                       EMTAGE, John, Spencer;
                       BODMER, Mark, William;
                       ATHWAL, Diljeet, Singh
PATENT ASSIGNEE(S):
                       CELLTECH LIMITED;
                       MORGAN, Susan, Adrienne;
                       EMTAGE, John, Spencer;
                       BODMER, Mark, William;
                       ATHWAL, Diljeet, Singh
LANGUAGE OF PUBL .:
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                               KIND DATE
                       NUMBER
                       WO 9429351 A2 19941222
DESIGNATED STATES
      W:
                       AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP
                       KE KG KP KR KZ LK LU LV MD MG MN MW NL NO NZ PL PT RO
                       RU SD SE SI SK TJ TT UA US UZ VN AT BE CH DE DK ES FR
                       GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML
                       MR NE SN TD TG
APPLICATION INFO.:
                       WO 1994-GB1290
                                           A 19940615
PRIORITY INFO.:
                       GB 1993-9312415.4
                                              19930616
                       GB 1994-9401597.1
                                               19940127
                       GB 1994-9402499.9 19940209
GB 1994-9406244.5 19940329
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The invention provides antibodies with altered ability to fix

complement. The invention further

well as in immunodiagnostics. These antibodies are constructed by fusing

ABEN

relates to pharmaceutical, therapeutic and diagnostic compositions containing said antibodies and to

methods of therapy and diagnosis using said antibodies. The invention additionally provides a method

of modulating the function of cell surface associated antigens using said antibodies. Also provided

are processes for preparing said antibodies.

ABFR L'invention concerne des anticorps presentant une capacite modifiee de fixation a un

complement. L'invention concerne, de plus, des compositions pharmaceutiques, therapeutiques et

diagnostiques contenant lesdits anticorps, ainsi que des procedes therapeutiques et diagnostiques

utilisant lesdits anticorps. Elle concerne, de plus, un procede de modulation de la fonction

d'antigenes associes a la surface d'une cellule au moyen desdits anticorps. Elle concerne egalement

des procedes de preparation desdits anticorps.

ANSWER 18 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1994028027 PCTFULL ED 20020513

TITLE (ENGLISH): METHODS AND MATERIALS FOR MODULATION OF THE

IMMUNOSUPPRESSIVE ACTIVITY AND TOXICITY OF MONOCLONAL

ANTIBODIES

PROCEDES ET MATIERES DE MODULATION DE L'ACTIVITE TITLE (FRENCH):

IMMUNODEPRESSIVE ET DE LA TOXICITE D'ANTICORPS

MONOCLONAUX

INVENTOR (S): BLUESTONE, Jeffrey, A.;

> ZIVIN, Robert, A.; JOLLIFFE, Linda

PATENT ASSIGNEE(S): ARCH DEVELOPMENT CORPORATION;

> BLUESTONE, Jeffrey, A.; ZIVIN, Robert, A.;

JOLLIFFE, Linda

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE -----WO 9428027 A1 19941208

DESIGNATED STATES

AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP W:

KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN

TD TG

A 19940601 APPLICATION INFO.: WO 1994-US6198 PRIORITY INFO.: US 1993-8/070,116 19930601

ABEN The binding specificity of the murine OKT3 has been transferred into a human antibody framework

in order to reduce its immunogenicity. Humanized anti-CD3 mAbs, such as gOKT3-5 and gOKT3-7, have

been shown to retain, in vitro, all the properties of native OKT3, including T cell activation which

has been correlated, in vivo, with the severe side-effects observed in transplant recipients after

the first administration of the mAb. Disclosed are modified versions of humanized anti-CD3 mAbs that

do not have the property of T cell activation. Further disclosed are

methods of using such mAbs.

ABFR On a transferre la specificite de liaison de l'anticorps monoclonal murin OKT3 sur un cadre

d'anticorps humain afin de reduire son immunogenecite. On a demontre que les anticorps monoclonaux

anti-CD3 adaptes au systeme humain, tels que gOKT3-5 et gOKT3-7,

conservent, in vitro, toutes les

proprietes de l'OKT3 natif, y compris l'activation des lymphocytes T que l'on a correle, in vivo,

avec les effets secondaires importants observes chez des receveurs de greffe, apres la premiere

administration de l'anticorps monoclonal. L'invention concerne egalement des versions modifiees

d'anticorps monoclonaux anti-CD3 adaptes au systeme humain, ne presentant pas la propriete

d'activation des lymphocytes T. En outre, l'invention concerne des procedes d'utilisation desdits

anticorps monoclonaux.

L9 ANSWER 19 OF 21 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1993019196 PCTFULL ED 20020513
TITLE (ENGLISH): ANTI-CD3 AGLYCOSYLATED IGG ANTIBODY
TITLE (FRENCH): ANTICORPS IGG ANTI-CD3 AGLYCOSYLES

INVENTOR(S):

BOLT, Sarah, Louise;

CLARK, Michael, Ronald;

GORMAN, Scott, David;

ROUTLEDGE, Edward, Graham;

WALDMANN, Herman

PATENT ASSIGNEE(S): BOLT, Sarah, Louise;

CLARK, Michael, Ronald; GORMAN, Scott, David; ROUTLEDGE, Edward, Graham;

WALDMANN, Herman

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W: AU CA JP KR US AT BE CH DE DK ES FR GB GR IE IT LU MC

NL SE

APPLICATION INFO.: WO 1992-GB1933 A 19921021 PRIORITY INFO.: GB 1992-9206422.9 19920324

ABEN Novel aglycosylated antibodies having a binding affinity for the CD3 antigen complex are of

value for use in therapy, particularly in immunosuppression.

ABFR De nouveaux anticorps aglycosyles ayant une affinite de liaison pour le complexe antigene CD3

sont employes utilement en therapie, particulierement dans les immuno suppressions.

L9 ANSWER 20 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1991009058 PCTFULL ED 20020513

TITLE (ENGLISH): THERAPEUTIC USES OF THE HYPERVARIABLE REGION OF

MONOCLONAL ANTIBODY M195 AND CONSTRUCTS THEREOF

TITLE (FRENCH): EMPLOIS THERAPEUTIQUES DE LA REGION HYPERVARIABLE DE

L'ANTICORPS MONOCLONAL M195 ET DE SES STRUCTURES

INVENTOR(S): SCHEINBERG, David, A.

PATENT ASSIGNEE(S): SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH;

SCHEINBERG, David, A.

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

NUMBER KIND DATE ------WO 9109058 A1 19910627

DESIGNATED STATES

W:

AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL SE US

APPLICATION INFO.: WO 1990-US7436 PRIORITY INFO.: US 1989-450,918

WO 1990-US7436 A 19901214 19891214

ABEN Therapeutic agents and methods for treating and diagnosing leukemia are provided. Such agents

comprise monoclonal antibody M195, a polypeptide capable of binding to the antigen of M195, or a

chimeric antibody such as a peptide, conjugated to a cytotoxic agent, e.g. a radioisotope or alone.

Methods for delivering genetic information to a targeted cell is also provided.

ABFR Agents et procedes therapeutiques de traitement et de diagnostic de la leucemie. Lesdits agents

comprennent l'anticorps monoclonal M195, un polypeptide capable de se lier a l'antigene du M195, ou

un anticorps chimerique tel qu'un peptide seul ou conjuge a un agent cytotoxique, par exemple un

radioisotope. L'invention concerne egalement des procedes d'acheminement d'informations genetiques a une cellule ciblee.

ANTICORPS A REGION CONSTANTE A MODIFICATION DE DOMAINE

ANSWER 21 OF 21 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1989007142 PCTFULL ED 20020513 TITLE (ENGLISH): DOMAIN-MODIFIED CONSTANT REGION

ANTIBODIES

MORRISON, Sherie, L.; INVENTOR(S):

OI, Vernon, T.

PATENT ASSIGNEE(S): MORRISON, Sherie, L.;

OI, Vernon, T.

LANGUAGE OF PUBL.:

TITLE (FRENCH):

English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE -----WO 8907142 A1 19890810

DESIGNATED STATES

W:

JΡ

WO 1989-US297 A 19890124 US 1988-152,741 19880205 APPLICATION INFO.: PRIORITY INFO.:

ABEN An antibody having at least one binding site region and a

domain-modified constant region is

provided wherein the domain-modified constant region

is a substitution, duplication, or deletion of

substantially all of the amino acids of at least one of the domains of the constant region. The

functional properties of the domain-modified constant

region antibodies are altered to enhance the

desired biological functions for a particular application. DNA sequences encoding constructs

expressing domain-modified constant region antibody heavy chains and cells expressing domain-modified constant region antibodies are also provided.

ABFR

Anticorps presentant au moins une region de site de liaison et une region constante a

modification de domaine, ou cette deuxieme region constitue une substitution, une duplication ou une

elimination essentiellement de tous les acides amines d'au moins l'un des domaines de la region

constante. Les proprietes fonctionnelles des anticorps a region constante a modification de domaine

sont modifiees pour ameliorer les fonctions biologiques desirees pour une application particuliere.

On decrit egalement des sequences d'ADN codant des structures qui expriment des chaines lourdes

d'anticorps a region constante a modification de domaine, ainsi que des cellules qui expriment des

anticorps a region constante a modification de domaine.

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        Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
                now available on STN
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        Aug 26
                Sequence searching in REGISTRY enhanced
                JAPIO has been reloaded and enhanced
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        Sep 03
NEWS 8 Sep 16
                Experimental properties added to the REGISTRY file
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA
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NEWS 12 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
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NEWS 17 Dec 17 TOXCENTER enhanced with additional content
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                Simultaneous left and right truncation added to COMPENDEX,
                ENERGY, INSPEC
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        Feb 13
                CANCERLIT is no longer being updated
        Feb 24 METADEX enhancements
NEWS 21
        Feb 24 PCTGEN now available on STN
NEWS 22
NEWS 23
        Feb 24 TEMA now available on STN
        Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 24
NEWS 25
        Feb 26 PCTFULL now contains images
                SDI PACKAGE for monthly delivery of multifile SDI results
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        Mar 20
                EVENTLINE will be removed from STN
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        Mar 24
                PATDPAFULL now available on STN
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        Mar 24
                Additional information for trade-named substances without
                structures available in REGISTRY
NEWS 30
        Apr 11
                Display formats in DGENE enhanced
NEWS 31
        Apr 14
                MEDLINE Reload
        Apr 17
NEWS 32
                Polymer searching in REGISTRY enhanced
                Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 33
        Jun 13
NEWS 34
        Apr 21
                New current-awareness alert (SDI) frequency in
                WPIDS/WPINDEX/WPIX
NEWS 35
        Apr 28
                RDISCLOSURE now available on STN
NEWS 36
                Pharmacokinetic information and systematic chemical names
        May 05
                added to PHAR
                MEDLINE file segment of TOXCENTER reloaded
NEWS 37
        May 15
NEWS 38
        May 15
                Supporter information for ENCOMPPAT and ENCOMPLIT updated
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NEWS 39 May 16 CHEMREACT will be removed from STN

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA

NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB

NEWS 43 Jun 06 PASCAL enhanced with additional data

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- 58 FILE PCTFULL
- 44 FILE USPATFULL
- 2 FILE WPIDS
- 2 FILE WPINDEX
- 3 FILE BIOSIS

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F5
          7 PROMT
F6
          6 CAPLUS
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          3 BIOSIS
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          3 BIOTECHNO
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          3 EMBASE
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          2 WPIDS
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          2 WPINDEX
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          2 ESBIOBASE
F13
          2 LIFESCI
2 MEDLINE
1 IFIPAT
1 PATDPAFULL
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          1 CABA
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          1 CONFSCI
F21
          1 DRUGU
          1 FEDRIP
F22
F23
           1 VETU
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COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 3.30 3.93

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FILE 'SCISEARCH' ENTERED AT 11:37:04 ON 23 JUN 2003 COPYRIGHT 2003 THOMSON ISI

=> s fcrp

L2 121 FCRP

=> s IgG

L3 332820 IGG

=> s protection receptor

L4 48 PROTECTION RECEPTOR

=> s protection receptor

=> s 14 and 12 and 13

L5 24 L4 AND L2 AND L3

=> dup rem 15

PROCESSING COMPLETED FOR L5

L6 15 DUP REM L5 (9 DUPLICATES REMOVED)

=> d ibib abs ind 1-15

L6 ANSWER 1 OF 15 USPATFULL

ACCESSION NUMBER: 2003:153626 USPATFULL

TITLE: ENHANCING THE CIRCULATING HALF LIFE OF ANTIBODY-BASED

FUSION PROTEINS

INVENTOR(S): GILLIES, STEPHEN, CARLISLE, MA, UNITED STATES

LO, KIN-MING, LEXINGTON, MA, UNITED STATES

LAN, YAN, BELMONT, MA, UNITED STATES

WESOLOWSKI, JOHN, WEYMOUTH, MA, UNITED STATES

NUMBER DATE

PRIORITY INFORMATION: US 1998-75887P 19980225 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125

HIGH STREET, BOSTON, MA, 02110

NUMBER OF CLAIMS: 26 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 7 Drawing Page(s)

LINE COUNT: 1022

Disclosed are methods for the genetic construction and expression of antibody-based fusion proteins with enhanced circulating half-lives. The fusion proteins of the present invention lack the ability to bind to immunoglobulin Fc receptors, either as a consequence of the antibody isotype used for fusion protein construction, or through directed mutagenesis of antibody isotypes that normally bind Fc receptors. The fusion proteins of the present invention may also contain a functional domain capable of binding an immunoglobulin protection

receptor.

INCL INCLM: 530/351.000

INCLS: 530/391.100 NCLM: 530/351.000

NCLS: 530/391.100 IC [7]

NCL

ICM: C07K016-46 ICS: C07K014-54

ANSWER 2 OF 15 USPATFULL

ACCESSION NUMBER: 2003:64303 USPATFULL

Expression technology for proteins containing a hybrid TITLE:

isotype antibody moiety

Gillies, Stephen D., Carlisle, MA, UNITED STATES INVENTOR(S):

> Way, Jeffrey, Cambridge, MA, UNITED STATES Lo, King-Ming, Lexington, MA, UNITED STATES

Lexigen Pharmaceuticals Corp., Lexington, MA (U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE US 2003044423 A1 US 2002-93958 A1 PATENT INFORMATION: APPLICATION INFO.: 20030306 20020307 (10)

> NUMBER DATE -----

US 2001-274096P 20010307 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125

HIGH STREET, BOSTON, MA, 02110

NUMBER OF CLAIMS: 28 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 4 Drawing Page(s)

2288 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are methods and compositions for efficiently expressing AB antibody fusion proteins. Antibody fusion proteins of the invention include a hybrid antibody moiety containing sequences from more than one type of antibody and/or mutant antibody sequences. Hybrid antibody fusion proteins of the invention may be produced at high levels and may combine functional properties characteristic of different antibody types in addition to functional properties of a non-antibody moiety.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/192.100

STN search for 09/256,156 NCLM: 424/192.100 NCL IC [7] ICM: A61K039-00 CHEMICAL ABSTRACTS INDEXING COPYRIGHT 2003 ACS ------PATENT KIND DATE ______ CA 137:246548 * WO 02072605 A2 20020919 OS * CA Indexing for this record included CC 15-3 (Immunochemistry) Section cross-reference(s): 2, 3, 7, 63 chimeric hybrid antibody Iq isotype immunocytokine immunofusin ST immunoligand Immunoglobulins ΙT (A; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Interleukin 14 Proteins (Acrp30; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT (CLC/CLF; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Immunoglobulins (G1: chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Immunoglobulins (G2; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Immunoglobulins (G3; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Immunoglobulins (G4; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Immunoglobulins (G: chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT (GLP-1 or glucagon-like protein; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Immunoglobulins (M; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Antitumor agents Cytotoxic agents Human Mammalia Molecular cloning Mouse Mutagenesis Protein sequences (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Chemokines Ciliary neurotrophic factor

Enzymes, biological studies

```
Hormones, animal, biological studies
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
ΙT
      Fusion proteins (chimeric proteins)
      Immunoglobulins
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Avidins
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      CD4 (antigen)
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      CTLA-4 (antigen)
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interferons
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      Interleukin 1 receptors
ΙT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
ΙT
      Interleukin 10
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
ΙT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 13
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      Interleukin 15
IT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      Interleukin 16
IT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 2
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 4
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 4 receptors
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 5
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
IT
      Interleukin 6
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
ΙT
      Interleukin 7
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
ΙT
      Interleukin receptors
```

(chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Lymphokines (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Lymphotoxin (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) Tumor necrosis factors IT (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ITAntigens Glycolipids Nucleic acids (chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) Immunoglobulins ΙT (fragments; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IΤ Immunoglobulins (heavy chains; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT (hybrid; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Cytokines Ligands (immuno-; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) TIChemokine receptors (immunofusins; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT (ligand-binding; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) Immunoglobulins ΙT (light chains; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT (obesity; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) Obesity IT (protein; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) ΙT Mutagenesis (site-directed, substitution; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Receptors (transmembrane; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Antigens (tumor-assocd.; chimeric proteins comprising hybrid isotype antibody, immunocytokines, immunofusins, or immunoligands for therapeutic use) IT Interferons (.alpha.; chimeric proteins comprising hybrid isotype antibody,

```
immunocytokines, immunofusins, or immunoligands for therapeutic use)
ΙT
      Interferons
        (.beta.; chimeric proteins comprising hybrid isotype antibody,
        immunocytokines, immunofusins, or immunoligands for therapeutic use)
IT
        (.gamma.; chimeric proteins comprising hybrid isotype antibody,
        immunocytokines, immunofusins, or immunoligands for therapeutic use)
     460772-95-6P
TТ
                   460772-96-7P
        (amino acid sequence; chimeric proteins comprising hybrid isotype
        antibody, immunocytokines, immunofusins, or immunoligands for
        therapeutic use)
      11096-26-7P, Erythropoietin
IT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      9001-99-4P, RNase
                         9002-72-6P, Growth hormone
                                                      9004-10-8P, Insulin,
IT
     biological studies
                          83869-56-1P, GM-CSF 143011-72-7P, G-CSF
      169494-85-3P, Leptin
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      65988-71-8, Ganglioside GD2
                                   80295-33-6, Complement Clq
IT
        (chimeric proteins comprising hybrid isotype antibody, immunocytokines,
        immunofusins, or immunoligands for therapeutic use)
      460773-86-8 460773-87-9 460773-88-0
                                               460773-89-1
                                                              460773-90-4
TΤ
                                 460773-93-7
                                                460773-94-8
                                                              460773-95-9
      460773-91-5 460773-92-6
      460773-96-0 460773-97-1 460773-98-2
                                                460773-99-3
                                                              460774-00-9
      460774-01-0 460774-02-1
                                 460774-03-2
                                                460774-04-3
                                                              460774-05-4
      460774-06-5
                   460774-07-6 460774-08-7
                                                460774-09-8
                                                              460774-10-1
      460774-11-2
        (unclaimed nucleotide sequence; chimeric proteins comprising hybrid
        isotype antibody, immunocytokines, immunofusins, or immunoligands for
        therapeutic use)
                                                              460706-76-7
IT
      106612-94-6
                   157079-60-2
                                  355367-80-5
                                                460706-75-6
                   460706-78-9
                                 460706-79-0
                                                460706-80-3
                                                              460706-81-4
      460706-77-8
                                  460706-84-7
                                                460706-85-8
                                                              460706-86-9
      460706-82-5
                   460706-83-6
      460706-87-0 460706-88-1
                                  460706-89-2
                                                460706-90-5
        (unclaimed sequence; chimeric proteins comprising hybrid isotype
        antibody, immunocytokines, immunofusins, or immunoligands for
        therapeutic use)
                                   COPYRIGHT 2003 Univentio
      ANSWER 3 OF 15
                         PCTFULL
                        2002072605 PCTFULL ED 20020927 EW 200238
ACCESSION NUMBER:
                        EXPRESSION TECHNOLOGY FOR PROTEINS CONTAINING A HYBRID
TITLE (ENGLISH):
                        ISOTYPE ANTIBODY MOIETY
                        TECHNIQUE D'EXPRESSION POUR DES PROTEINES CONTENANT UN
TITLE (FRENCH):
                        FRAGMENT D'ANTICORPS ISOTYPE CHIMERIQUE
INVENTOR (S):
                        GILLIES, Stephen, D., 159 Sunset Road, Carlisle, Ma
                        01741, US;
                        WAY, Jeffrey, 108 Fayerweather Street, Cambridge, MA
                        02138, US
                        LEXIGEN PHARMACEUTICALS CORP., 125 Hartwell Avenue,
PATENT ASSIGNEE(S):
                        Lexington, MA 02173, US [US, US]
                        WALLER, Patrick, R., H., Testa, Hurwitz & Thibeault,
AGENT:
                        L.L.P., High Street Tower, 125 High Street, Boston, MA
                        02110, US
LANGUAGE OF FILING:
                        English
                        English
LANGUAGE OF PUBL.:
DOCUMENT TYPE:
                        Patent
PATENT INFORMATION:
```

KIND

DATE

NUMBER

WO 2002072605 A2 20020919

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE RW (EPO):

TR

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

RW (OAPI):
APPLICATION INFO.: WO 2002-US7011 A 20020307 US 2001-60/274,096 PRIORITY INFO.: 20010307

ABEN Disclosed are methods and compositions for efficiently expressing antibody fusion proteins. Antibody fusion proteins of the invention include a hybrid antibody moiety containing sequences from more than one type of antibody and/or mutant antibody sequences. Hybrid antibody fusion proteins of the invention may be produced at high levels and may combine functional properties characteristic of different antibody types

in addition to functional properties of a non-antibody moiety.

L'invention concerne des procedes et des compositions permettant ABFR d'exprimer efficacement des proteines hybrides d'anticorps. Les proteines hybrides d'anticorps de cette invention comprennent un fragment d'anticorps chimerique contenant des sequences de plus d'un type de sequences d'anticorps et/ou d'anticorps mutants. Les proteines hybrides d'anticorps chimerique de cette invention peuvent etre produites a des niveaux eleves et peuvent combiner des proprietes fonctionnelles caracteristiques de differents types d'anticorps a des proprietes fonctionnelles d'un fragment qui n'est pas d'un anticorps.

ANSWER 4 OF 15 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 2002043658 PCTFULL ED 20020624 EW 200223 FCRN-BASED THERAPEUTICS FOR THE TREATMENT OF TITLE (ENGLISH):

AUTO-IMMUNE DISORDERS

TRAITEMENT A BASE DE FCRN POUR TROUBLES AUTOIMMUNS TITLE (FRENCH): INVENTOR(S): ROOPENIAN, Derry, Box 29, Locust Lane, Salisbury Cove,

ME 04672, US

PATENT ASSIGNEE(S): THE JACKSON LABORATORY, 600 Main Street, Bar Harbor, ME

04609-1500, US [US, US]

FARRELL, Kevin, M., P.O. Box 999, York Harbor, ME AGENT:

03911, US

LANGUAGE OF FILING: English LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

KIND DATE NUMBER WO 2002043658 A2 20020606

DESIGNATED STATES

CA JP W:

AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE RW (EPO):

TR

WO 2001-US44166 A 20011106 APPLICATION INFO.: US 2000-60/246,207 US 2001-60/266,649 PRIORITY INFO.: 20001106 20010206

Disclosed is a transgenic knockout mouse whose genome comprises a ABEN homozygous disruption in its endogenous FcRn gene, wherein said

homozygous disruption prevents the expression of a functional FcRn protein, resulting in a transgenic knockout mouse in which exogenously administered IqG1 exhibits a subtantially shorter half-life, as compared to the half-life of exogenously administered IqG1 in a wild-type mouse. Also disclosed is a transgenic knockout mouse whose genome comprises a homozygous disruption in its endogenous FcRn gene, wherein said homozygous disruption prevents the expression of a functional FcRn protein, resulting in a transgenic knockout mouse which is unable to absorb maternal IgG in the prenatal or neonatal stage of development. Methods of using the transgenic knockout mouse, and cells derived therefrom, are also disclosed.

Cette invention concerne une souris transgenique knockout dont le genome ABFR comprend une disruption homozygote dans son gene FcRn endogene. Cette disruption homozygote empeche l'expression d'une proteine FcRn fonctionnelle, la consequence etant que chez la souris transgenique knockout, la demi-vie d'IgG1 administre de maniere exogene est sensiblement plus courte que celle d'un IgG1 administre de la meme maniere chez une souris sauvage. L'invention concerne egalement une souris transgenique knockout dont le genome comprend dans son gene FcRn endogene une disruption homozygote qui empeche l'expression d'une proteine FcRn fonctionnelle, avec pour consequence l'incapacite chez cette souris d'absorber l'IgG maternel au stade prenatal ou neonatal du developpement. L'invention porte egalement sur des methodes d'utilisation de cette souris transgenique knockout et des cellules prelevees sur cette souris.

ANSWER 5 OF 15 USPATFULL

ACCESSION NUMBER:

2002:266428 USPATFULL

TITLE:

Enhancing the circulating half-life of antibody-based

fusion proteins

INVENTOR(S):

Gillies, Stephen D., Carlisle, MA, UNITED STATES

Burger, Christa, Darmstadt, GERMANY, FEDERAL REPUBLIC

Lo, Kin-Ming, Lexington, MA, UNITED STATES

NUMBER KIND DATE _______ US 2002147311 A1 20021010 US 2001-780668 A1 20010209 (9)

PATENT INFORMATION: APPLICATION INFO.:

> NUMBER DATE _____

PRIORITY INFORMATION:

US 2000-181768P 20000211 (60)

DOCUMENT TYPE: Utility FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

TESTA, HURWITZ & THIBEAULT, LLP, HIGH STREET TOWER, 125

HIGH STREET, BOSTON, MA, 02110

NUMBER OF CLAIMS: 47 1 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 6 Drawing Page(s)

LINE COUNT: 1491

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Disclosed are compositions and methods for enhancing the circulating AΒ half-life of antibody-based fusion proteins. Disclosed methods and compositions rely on altering the amino acid sequence of the junction region between the antibody moiety and the fused protein moiety in an antibody-based fusion protein. An antibody-based fusion protein with an altered amino acid sequence in the junction region has a greater circulating half-life when administered to a mammal. Disclosed methods

and compositions are particularly useful for reducing tumor size and metastasis in a mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 530/387.100 NCL NCLM: 530/387.100

IC [7]

ICM: C07K016-00

CHEMICAL ABSTRACTS INDEXING COPYRIGHT 2003 ACS

PATENT KIND DATE

OS CA 135:179712 * WO 0158957 A2 20010816

* CA Indexing for this record included

CC 15-3 (Immunochemistry)

Section cross-reference(s): 1, 2

ST antibody fusion protein pharmacokinetics

IT Antigens

(17-1A; enhancement of circulatory half-life of antibody fusion protein directed to)

IT Immunoglobulins

(G1, monoclonal, fusion products; enhancement of circulatory half-life of)

IT Immunoglobulins

(G2, monoclonal, fusion products; enhancement of circulatory half-life of)

IT Immunoglobulins

(G3, monoclonal, fusion products; enhancement of circulatory half-life of)

IT Immunoglobulins

(G4, monoclonal, fusion products; enhancement of circulatory half-life of)

IT Immunoglobulin receptors

(IgG type I; enhanced circulatory half-life of antibody-based fusion proteins in relation to reduced affinity for)

IT Immunoglobulin receptors

(IgG type II; enhanced circulatory half-life of antibody-based fusion proteins in relation to reduced affinity for)

IT Immunoglobulin receptors

(IgG type III; enhanced circulatory half-life of antibody-based fusion proteins in relation to reduced affinity for)

IT Antitumor agents

(antibody-based fusion proteins with enhanced circulatory half-life)

IT Fusion proteins (chimeric proteins)

(antibody-based; enhancement of circulatory half-life of)

IT CD4 (antigen)

CTLA-4 (antigen)

Cytokines

Interleukin 2

Interleukin receptors

Interleukins

Lymphokines

Lymphotoxin

Tumor necrosis factor receptors

Tumor necrosis factors

(fusion products, with antibodies; enhancement of circulatory half-life of)

IT Drug delivery systems

```
(immunotoxins; enhancement of circulatory half-life of)
IT
     Antitumor agents
        (metastasis; antibody-based fusion proteins with enhanced circulatory
       half-life)
IT
     Immunoglobulin receptors
        (neonatal; enhanced circulatory half-life of antibody-based fusion
       proteins in relation to reduced affinity for)
      Proteins, specific or class
ΙT
        (secretory, fusion products, with antibodies; enhancement of
       circulatory half-life of)
ΙT
     Antibodies
        (single chain, scFv, fusion products; enhancement of circulatory
       half-life of)
ΙT
     Mutagenesis
        (site-directed; in prepn. of antibody-based fusion proteins with
       enhanced circulatory half-life)
     83869-56-1D, GM-CSF, antibody fusion products
ΙT
        (enhancement of circulatory half-life of)
     65988-71-8, ganglioside GD2
IT
        (enhancement of circulatory half-life of antibody fusion protein
       directed to)
ΙT
     355484-24-1 355484-25-2 355484-26-3
                                              355484-27-4 355484-28-5
     355484-29-6 355484-30-9 355484-31-0 355484-32-1 355484-33-2
     355484-34-3 355484-35-4 355484-36-5 355484-37-6 355484-38-7
     355484-39-8 355484-40-1 355484-41-2 355484-42-3 355484-43-4
                                              355484-47-8 355484-48-9
     355484-44-5 355484-45-6 355484-46-7
     355484-49-0 355484-50-3 355484-51-4
        (unclaimed nucleotide sequence; enhancing the circulating half-life of
       antibody-based fusion proteins)
ΙT
     355367-79-2 355367-80-5
                                 355367-81-6
                                              355367-82-7
     355367-84-9 355367-85-0
        (unclaimed sequence; enhancing the circulating half-life of
       antibody-based fusion proteins)
    ANSWER 6 OF 15 USPATFULL
ACCESSION NUMBER:
                       2002:258804 USPATFULL
TITLE:
                       GENERATION OF MODIFIED MOLECULES WITH INCREASED SERUM
                       HALF-LIVES
                       GALLO, MICHAEL, SAN JOSE, CA, UNITED STATES
INVENTOR(S):
                       JUNGHANS, RICHARD, BOSTON, MA, UNITED STATES
                       FOORD, ORIT, FOSTER CITY, CA, UNITED STATES
                            NUMBER KIND DATE
                       US 2002142374 A1 20021003
US 1999-375924 A1 19990817
PATENT INFORMATION:
APPLICATION INFO.:
                                              19990817 (9)
                            NUMBER DATE
                       -----
                       US 1998-96868P 19980817 (60)
PRIORITY INFORMATION:
DOCUMENT TYPE:
                       Utility
FILE SEGMENT:
                       APPLICATION
LEGAL REPRESENTATIVE: FISH & NEAVE, 1251 AVENUE OF THE AMERICAS, 50TH FLOOR,
                       NEW YORK, NY, 10020-1105
NUMBER OF CLAIMS:
                       11
EXEMPLARY CLAIM:
NUMBER OF DRAWINGS:
                       3 Drawing Page(s)
LINE COUNT:
                       2060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

AB In accordance with the present invention, there are provided methods for the extension of serum half-lives of proteinaceous molecules, particularly antibody molecules, and compositions of molecules modified in accordance with the methods of the invention. In accordance with a first aspect of the present invention, there is provided a method of modifying the half-life of an antibody through providing an antibody containing an FcRn binding domain or the genes encoding such antibody and physically linking the antibody or the antibody as encoded to a second FcRn binding domain. In accordance with a second aspect of the present invention, there is provided a molecule that contains at least two distinct FcRn binding moieties.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/069.100

INCLS: 435/069.600; 530/387.300; 530/388.100; 530/388.230

NCL NCLM: 435/069.100

NCLS: 435/069.600; 530/387.300; 530/388.100; 530/388.230

IC [7]

ICM: C12P021-06

ICS: C12P021-04; C12P021-08; C07K016-00

CHEMICAL ABSTRACTS INDEXING COPYRIGHT 2003 ACS

PATENT KIND DATE

OS CA 132:193257 * WO 0009560 A2 20000224 * CA Indexing for this record included

CC 15-3 (Immunochemistry)

Section cross-reference(s): 3

ST antibody Fc receptor binding domain IL8

IT Immunoglobulins

(G, heavy chain; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Immunoglobulins

(G1; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Immunoglobulins

 $(G2; \ recombinant \ proteins \ or \ antibodies \ contg.$ FcR binding domain for increasing serum half-life)

IT Immunoglobulins

(G4; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Immunoglobulins

(M, heavy chain; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Immunoglobulin receptors

(binding domain; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Immunoglobulins

(heavy chains; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Antibodies

(monoclonal; recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Blood serum

Mammal (Mammalia)

Molecular cloning

(recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Antibodies

Gene, animal

(recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Interleukin 8

(recombinant proteins or antibodies contg. FcR binding domain for increasing serum half-life)

IT Proteins, general, biological studies

(recombinant; recombinant proteins or antibodies contg. FcR binding domain or genes encoding them for increasing serum half-life for therapy)

IT 259651-47-3, 5: PN: WO0009560 PAGE: 47 unclaimed DNA 259651-48-4, 6: PN: WO0009560 PAGE: 47 unclaimed DNA 259651-49-5, 7: PN: WO0009560 FIGURE: 2 unclaimed DNA 259651-50-8, 8: PN: WO0009560 FIGURE: 2 unclaimed DNA 259651-51-9, 9: PN: WO0009560 FIGURE: 2 unclaimed DNA 259651-52-0

(unclaimed nucleotide sequence; generation of modified mols. with increased serum half-lives)

IT 157079-60-2 255372-54-4 259533-10-3 259533-13-6 (unclaimed sequence; generation of modified mols. with increased serum half-lives)

L6 ANSWER 7 OF 15 USPATFULL

ACCESSION NUMBER:

PATENT ASSIGNEE(S):

2002:252898 USPATFULL

TITLE:

FcRn-based therapeutics for the treatment of

auto-immune disorders

INVENTOR(S):

Roopenian, Derry, Salisbury Cove, ME, UNITED STATES
The Jackson Laboratory, Bar Harbour, ME, UNITED STATES,

04609-1500 (U.S. corporation)

NUMBER DATE

PRIORITY INFORMATION:

US 2001-266649P 20010206 (60) US 2000-246207P 20001106 (60)

DOCUMENT TYPE:

Utility

FILE SEGMENT:

APPLICATION

LEGAL REPRESENTATIVE:

Kevin M. Farrell, Kevin M. Farrell, P.C., 18 York

Street, P.O. Box 999, York Harbour, ME, 03911

NUMBER OF CLAIMS:

80

EXEMPLARY CLAIM:

8 Drawing Page(s)

NUMBER OF DRAWINGS: LINE COUNT:

1895

Disclosed is a transgenic knockout mouse whose genome comprises a homozygous disruption in its endogenous FcRn gene, wherein said homozygous disruption prevents the expression of a functional FcRn protein, resulting in a transgenic knockout mouse in which exogenously administered IgG1 exhibits a substantially shorter half-life, as compared to the half-life of exogenously administered IgG1 in a wild-type mouse. Also disclosed is a transgenic knockout mouse whose genome comprises a homozygous disruption in its endogenous FcRn gene, wherein said homozygous disruption prevents the expression of a functional FcRn protein, resulting in a transgenic knockout mouse which is unable to absorb maternal IgG in the prenatal or neonatal stage of development Methods of using the transgenic knockout mouse, and

cells derived therefrom, are also disclosed.

INCL INCLM: 800/018.000

INCLS: 800/003.000

NCL NCLM: 800/018.000

NCLS: 800/003.000

IC [7]

ICM: A01K067-027

L6 ANSWER 8 OF 15 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 2001058957 PCTFULL ED 20020827

TITLE (ENGLISH): ENHANCING THE CIRCULATING HALF-LIFE OF ANTIBODY-BASED

FUSION PROTEINS

TITLE (FRENCH): AMELIORATION DE LA DEMI-VIE CIRCULANTE DE PROTEINES DE

FUSION A BASE D'ANTICORPS

INVENTOR(S): GILLIES, Stephen, D.;

BURGER, Christa; LO, Kin, Ming

PATENT ASSIGNEE(S): LEXIGEN PHARMACEUTICALS CORP.

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE
-----WO 2001058957 A2 20010816

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DM ES ES ES FI GB GD GE GH GM HR HU ID IL IN IN IS JP KE KG KP KR KZ LC LK LR LS LS LT LU LV MA MD MG MK MN MX MZ NO NZ PL PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG

CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 2001-US4455 A 20010209
PRIORITY INFO.: US 2000-60/181,768 20000211

ABEN Disclosed are compositions and methods for enhancing the circulating half-life of antibody-based fusion proteins. Disclosed methods and compositions rely on altering the amino acid sequence of the junction region between the antibody moiety and the fused protein moiety in an antibody-based fusion protein. An antibody-based fusion protein with an altered amino acid sequence in the junction region has a greater circulating half-life when administered to a mammal. Disclosed methods and compositions are particularly useful for reducing tumor size and metastasis in a mammal.

ABFR L'invention concerne des compositions et des methodes permettant d'ameliorer la demi-vie circulante de proteines de fusion a base d'anticorps. Ces methodes et ces compositions consistent a modifier la sequence d'acide amine de la region de jonction entre la fraction d'anticorps et la fraction de proteine fusionnee dans une proteine de fusion a base d'anticorps. Une proteine de fusion a base d'anticorps comportant une sequence d'acide amine modifiee dans sa region de jonction possede une demi-vie circulante plus longue lorsqu'elle administree a un mammifere. Ces methodes et ces compositions sont notamment utiles pour reduire la taille des tumeurs et les metastases chez un mammifere.

ICM C07K019-00

ICS G01N033-68; C07K016-00; C07K016-28; C07K014-52; C07K014-525; C07K014-55

PCTFULL

```
ANSWER 9 OF 15
ACCESSION NUMBER:
                       2000009560 PCTFULL ED 20020515
TITLE (ENGLISH):
                       GENERATION OF MODIFIED MOLECULES WITH INCREASED SERUM
                       HALF-LIVES
TITLE (FRENCH):
                       PRODUCTION DE MOLECULES MODIFIEES AVEC DEMI-VIE SERIQUE
                       PROLONGEE
INVENTOR(S):
                       GALLO, Michael;
                       JUNGHANS, Richard;
                       FOORD, Orit
                       ABGENIX, INC.
PATENT ASSIGNEE(S):
LANGUAGE OF PUBL.:
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                       NUMBER
                                         KIND
                                                 DATE
                        -----
                       WO 2000009560 A2 20000224
DESIGNATED STATES
                       AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE
      W :
                       DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE
                       KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO
                       NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ
                       VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG
                       KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT
                       LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN
                       TD TG
                                           A 19990817
APPLICATION INFO .:
                       WO 1999-US18777
PRIORITY INFO.:
                       US 1998-60/096,868 19980817
      In accordance with the present invention, there are provided methods for
       the extension of serum
      half-lives of proteinaceous molecules, particularly antibody molecules,
       and compositions of
      molecules modified in accordance with the methods of the invention. In
       accordance with a first
       aspect of the present invention, there is provided a method of modifying
       the half-life of an
       antibody through providing an antibody containing an FcRn binding domain
       or the genes encoding such
       antibody and physically linking the antibody or the antibody as encoded
       to a second FcRn binding
       domain. In accordance with a second aspect of the present invention,
       there is provided a molecule
       that contains at least two distinct FcRn binding moieties.
      La presente invention concerne des procedes d'extension des demi-vies
ABFR
       seriques de molecules
       proteiniques, particulierement de molecules d'anticorps, cette invention
       concernant egalement des
       compositions de molecules modifiees selon les procedes de l'invention.
       Un premier aspect de
       l'invention concerne un procede de modification de la demi-vie d'un
       anticorps grace a un anticorps
       comprenant un domaine de liaison FcRn, ou aux genes codant un tel
       anticorps fixant physiquement cet
       anticorps ou l'anticorps ainsi code sur un second domaine de liaison
       FcRn. Un second aspect de
       l'invention concerne une molecule renfermant au moins deux fractions de
       liaison FcRn distinctes.
I CM
       C07K016-42
       C07K016-24; C12N015-19; C12N015-66
ICS
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ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS
                                                       DUPLICATE 1
ACCESSION NUMBER:
                        2000:445482 CAPLUS
DOCUMENT NUMBER:
                         133:175911
                         The role of the Brambell receptor (FcRB) in liver:
TITLE:
                         protection of endocytosed immunoglobulin G (
                         IgG) from catabolism in hepatocytes rather
                         than transport of IgG to bile
AUTHOR(S):
                         Telleman, P.; Junghans, R. P.
CORPORATE SOURCE:
                         Biotherapeutics Development Lab, Harvard Institute of
                         Human Genetics, Harvard Medical School, Boston, MA,
                         02215, USA
SOURCE:
                         Immunology (2000), 100(2), 245-251
                         CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER:
                         Blackwell Science Ltd.
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     The Brambell receptor (FcRB) mediates functions of both IqG
     transport, transmitting immunity from mother to young, and IgG
     protection, making IgG the longest surviving of all plasma
     proteins. Reflecting its role as transport receptor (termed FcRn, for
     neonatal rat intestine, the tissue from which it was first cloned), FcRB
     is expressed antenatally in the rabbit, mouse and rat fetal yolk sac and
     in human placental syncytiotrophoblasts, and neonatally in the intestinal
     epithelium of mice and rats. Reflecting its role as protection
     receptor (FcRp), FcRB is expressed in the vascular
     endothelium throughout life, where it protects IqG from the
     on-going catabolic activities of this tissue. FcRB detected in
    hepatocytes was hypothesized to mediate transport of IgG from
     serum to bile, thus potentially extending the transport expression (FcRn)
     of this receptor beyond the perinatal period. The authors' results show
     serum-to-bile transport of IgG to be unaffected in mice
     functionally deleted for FcRB. Accordingly, the hypothesis is rejected
     that FcRB functions as transport receptor (FcRn) in liver. The default
     conclusion is that FcRB in hepatocytes functions as FcRp,
     serving to protect IqG from catabolism in hepatocytes that
     accompanies the endocytic activity of these cells. The authors conclude
     that there remains to date no evidence of an FcRn-like transport function
     of the Brambell receptor beyond the perinatal period, after which the
     FCRp function of the receptor predominates, paralleling the
     endocytic activities of the assocd. tissues.
CC
     15-3 (Immunochemistry)
ST
     Brambell receptor endocytosis IgG hepatocyte; catabolism
     IgG liver FcRn receptor
IT
     Immunoglobulins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (G; Brambell receptor in protection of endocytosed IgG from
        catabolism)
TT
    Liver
        (hepatocyte; Brambell receptor in protection of endocytosed IgG
        from catabolism)
     Immunity
IT
        (humoral; Brambell receptor in protection of endocytosed IgG
        from catabolism in relation to)
IT
     Immunoglobulin receptors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (neonatal; in protection of endocytosed IgG from catabolism)
                               THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                        50
```

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 15 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1999043713 PCTFULL ED 20020515

TITLE (ENGLISH): ENHANCING THE CIRCULATING HALF-LIFE OF ANTIBODY-BASED

FUSION PROTEINS

TITLE (FRENCH): AMELIORATION DE LA DEMI-VIE CIRCULANTE DE PROTEINES

HYBRIDES A BASE D'ANTICORPS

INVENTOR(S): GILLIES, Stephen, D.;

LO, Kin-Ming; LAN, Yan;

WESOLOWSKI, John

PATENT ASSIGNEE(S): LEXIGEN PHARMACEUTICALS CORPORATION

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BB BG BR BY CA CH CN CU CZ DE DK EE BS FI GB GD GC GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1999-US3966 A 19990224 PRIORITY INFO.: US 1998-60/075,887 19980225

ABEN Disclosed are methods for the genetic construction and expression of antibody-based fusion

proteins with enhanced circulating half-lives. The fusion proteins of the present invention lack the

ability to bind to immunoglobulin Fc receptors, either as a consequence of the antibody isotype used

for fusion protein construction, or through directed mutagenesis of antibody isotypes that normally

bind Fc receptors. The fusion proteins of the present invention may also contain a functional domain

capable of binding an immunoglobulin $\ensuremath{\mbox{{\bf protection}}}$

receptor.

ABFR On decrit des procedes de construction genetique et d'expression de proteines hybrides a base

d'anticorps ayant une demi-vie circulante amelioree. Les proteines hybrides de l'invention sont

incapables de se lier aux recepteurs pour le fragment Fc des immunoglobulines, soit en consequence

de l'utilisation de l'isotype des anticorps pour construire la proteine hybride, soit par mutagenese

dirigee des isotypes des anticorps qui se lient normalement aux recepteurs pour le fragment Fc. Les

proteines hybrides de l'invention peuvent egalement contenir un domaine fonctionnel capable de lier

un recepteur de protection des immunoglobulines.

ICM C07K019-00

ICS C07K014-52; C07K014-55; C07K014-705; C07K014-73

L6 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2 ACCESSION NUMBER: 1997:757035 CAPLUS

Page 19

DOCUMENT NUMBER: 128:33795

TITLE: Physiologically active molecules modified with

FcRp-binding peptide for extending half-lives

and for therapy

INVENTOR(S):
Junghans, Richard P.

PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Inc., USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 9743316 A1 19971120 WO 1997-US7707 19970506

W: CA, JP

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE PRIORITY APPLN. INFO.:

US 1996-17249P P 19960510
US 1997-841815 A 19970505

AB The present invention is drawn to physiol. active mols. which have extended half-lives in the circulatory system of a subject and have a structure which is modified to include amino acid sequence which binds to IgG protection receptor FcRp but

does not bind to an Fc receptor which mediates immune effects. The FcRp-binding peptide or protein is an Ig or all or a portion of IgG3, IgA, IgD, IgE, and IgM. Compns. which include these mols., methods of producing the mols., and methods of using the mols. to treat subjects are also disclosed. By modifying the physiol. active mols. in this manner, the invention takes advantage of the discovery that the FcRp and the FcRn are the same receptor and that modifying physiol. active mols. such that they are capable of binding the IgG protection receptor FcRp allows

these mols. to escape lysosomal catabolism and remain in the circulation of a subject for longer periods of time. Demonstrated were modification of IgM, IgA, hepatitis B surface antigen, HIV envelope protein gp120, glycophorin A, interleukin 10 and TGF.beta. for treatment.

IC ICM C07K016-46

ICS A61K039-00; A61K039-395

CC 15-3 (Immunochemistry)

ST modified physiol active mol FcRp binding; Ig antigen lymphokine FcRp binding

IT Glycophorins

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(A, modified; physiol. active mols. modified with FcRp

-binding peptide for extending half-lives and for treatment)

IT Immunoglobulins

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (A; physiol. active mols. modified with FcRp-binding peptide

for extending half-lives and for treatment)

IT Immunoglobulins

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (D; physiol. active mols. modified with FcRp-binding peptide for extending half-lives and for treatment)

IT Immunoglobulins

RL: BPR (Biological process); BSU (Biological study, unclassified); THU

```
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (E; physiol. active mols. modified with FcRp-binding peptide
        for extending half-lives and for treatment)
    Immunoglobulin receptors
TΤ
    RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (FcRn (Ig fragment Fc receptor, neonatal), FcRp equiv.;
       physiol. active mols. modified with FcRp-binding peptide for
        extending half-lives and for treatment)
ΙT
    Immunoglobulins
    RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (G3; physiol. active mols. modified with FcRp-binding peptide
        for extending half-lives and for treatment)
ΙT
    Immunoglobulins
    RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (M; physiol. active mols. modified with FcRp-binding peptide
        for extending half-lives and for treatment)
ΙT
    Envelope proteins
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
    study); PREP (Preparation); USES (Uses)
        (qp120env, modified; physiol. active mols. modified with FcRp
        -binding peptide for extending half-lives and for treatment)
IT
    Antigens
    RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (hepatitis B surface, modified; physiol. active mols. modified with
        FcRp-binding peptide for extending half-lives and for
        treatment)
    Microorganism
IT
        (infection; physiol. active mols. modified with FcRp-binding
        peptide for extending half-lives and for treatment)
ΙT
     Interleukin 10
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (modified; physiol. active mols. modified with FcRp-binding
        peptide for extending half-lives and for treatment)
IT
    Autoimmune disease
     Human immunodeficiency virus
    Malaria
    Neoplasm
     Plasmodium falciparum
     Sepsis
     Vaccines
     Wiskott-Aldrich syndrome
        (physiol. active mols. modified with FcRp-binding peptide for
        extending half-lives and for treatment)
ΙT
     Immunoglobulins
     RL: BPR (Biological process); BSU (Biological study, unclassified); THU
     (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
        (physiol. active mols. modified with FcRp-binding peptide for
        extending half-lives and for treatment)
TΤ
     Molecules
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (physiol. active; physiol. active mols. modified with FCRp
        -binding peptide for extending half-lives and for treatment)
     Gram-negative bacteria
ΙT
```

ΤT

(sepsis; physiol. active mols. modified with FCRp-binding peptide for extending half-lives and for treatment)

IT Transforming growth factors

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(.beta.-, modified; physiol. active mols. modified with FcRp -binding peptide for extending half-lives and for treatment)

105052-10-6 199528-57-9 199528-58-0 199528-59-1 199528-60-4 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (physiol. active mols. modified with FcRp-binding peptide for extending half-lives and for treatment)

L6 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 3

ACCESSION NUMBER: 1996:327031 CAPLUS

DOCUMENT NUMBER: 125:7965

TITLE: The protection receptor for

IgG catabolism is the .beta.2-microglobulin-

containing neonatal intestinal transport receptor

AUTHOR(S): Junghans, R. P.; Anderson, C. L.

CORPORATE SOURCE: Biotherapeutics Development Lab, Harvard Med. Sch.,

Boston, MA, 02215, USA

SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (1996), 93(11), 5512-5516

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal LANGUAGE: English

To explain the long survival of IgG relative to other plasma proteins and its pattern of increased fractional catabolism with high concns. of IgG, Brambell et al. (Nature, 1964) postulated specific IgG "protection receptors" (FcRp) that would bind IqG in pinocytic vacuoles and redirect is transport to the circulation; when the ${\tt FcRp}$ was satd., the excess unbound IgG then would pass to unrestricted lysosomal catabolism. Brambell subsequently postulated the neonatal gut transport receptor (FcRn) and showed its similar saturable character. FcRn was recently cloned but FcRp has not been identified. Using a genetic knockout that disrupts the FcRn and intestinal IgG transport, the authors show that this lesion also disrupts the IqG protection receptor, supporting the identity of these two receptors. IgG catabolism was 10-fold faster and IgG levels were correspondingly lower in mutant than in wild-type mice, whereas IgA was the same between groups, demonstrating the specific effects on the IgG system. Disruption of the FcRp in the mutant mice was also shown to abrogate the classical pattern of decreased IgG survival with higher IgG concn. Finally, studies in normal mice with monomeric antigen-antibody complexes showed differential catabolism in which antigen dissocs. in the endosome and passes to the lysosome, whereas the assocd. antibody is returned to circulation; in mutant mice, differential catabolism was lost and the whole complex cleared at the same accelerated rate as albumin, showing the central role of the FcRp to the differential catabolism mechanism. Thus, the same receptor protein that mediates the function of the FcRn transiently in the neonate is shown to have its functionally dominant expression as the FcRp throughout life, resolving a longstanding mystery of the identity of the receptor for the protection of IqG. This result also identifies an important new member of the class of recycling surface receptors and enables the design of protein adaptations to exploit this mechanism to improve survivals of other

STN search for 09/256,156 therapeutic proteins in vivo. CC 15-3 (Immunochemistry) ST protection receptor IgG beta2 microglobulin intestine ΙT Biological transport Circulation Intestine Lysosome Mouse Newborn (protection receptor for IgG catabolism in circulation is .beta.2-microglobulin-contq. neonatal intestinal transport receptor) IT Immune complexes RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (protection receptor for IgG catabolism in circulation is .beta.2-microglobulin-contg. neonatal intestinal transport receptor) ΙT Receptors RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (protection; protection receptor for IgG catabolism in circulation is .beta.2-microglobulin-contg. neonatal intestinal transport receptor) IT Immunoglobulins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (G, protection receptor for IgG catabolism in circulation is .beta.2-microglobulin-contg. neonatal intestinal transport receptor) IT Organelle (endocytic vesicle, protection receptor for **IgG** catabolism in circulation is .beta.2-microglobulin-contq. neonatal intestinal transport receptor) TT Microglobulins occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

RL: BAC (Biological activity or effector, except adverse); BOC (Biological

(.beta.2-, protection receptor for IgG

catabolism in circulation is .beta.2-microglobulin-contg. neonatal intestinal transport receptor)

L6 ANSWER 14 OF 15 SCISEARCH COPYRIGHT 2003 THOMSON ISI

ACCESSION NUMBER: 96:398998 SCISEARCH

THE GENUINE ARTICLE: UK861

TITLE: THE BRAMBELL PROTECTION RECEPTOR (

FCRP) FOR IGG CATABOLISM IS THE NEONATAL

INTESTINAL TRANSPORT RECEPTOR (FCRN)

AUTHOR: JUNGHANS R P (Reprint); ZHENG G; ANDERSON C L; WATTERS J M HARVARD UNIV, SCH MED, NEW ENGLAND DEACONESS HOSP, DEPT CORPORATE SOURCE:

MED, BIOTHERAPEUT DEV LAB, BOSTON, MA, 02215; OHIO STATE UNIV, DEPT INTERNAL MED, COLUMBUS, MS, 00000; OHIO STATE UNIV, DEPT MOLEC GENET & MED BIOCHEM, COLUMBUS, MS, 00000

COUNTRY OF AUTHOR: USA

SOURCE: FASEB JOURNAL, (30 APR 1996) Vol. 10, No. 6, pp. 1737.

ISSN: 0892-6638.

DOCUMENT TYPE: Conference; Journal

FILE SEGMENT:

LIFE

LANGUAGE:

ENGLISH

REFERENCE COUNT:

No References

BIOLOGY; BIOCHEMISTRY & MOLECULAR BIOLOGY

ANSWER 15 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. ACCESSION NUMBER:

1996:309200 BIOSIS

DOCUMENT NUMBER:

PREV199699031556

TITLE:

The Brambell protection receptor (

FcRp) for IgG catabolism is the neo-natal

intestinal transport receptor (FcRn.

AUTHOR (S):

Junghans, R. P. (1); Zheng, G. (1); Anderson, C. L.;

Watters, J. M. (1)

CORPORATE SOURCE:

(1) Biotherapeutics Dev. Lab., Dep. Med., Harv. Med. Sch.,

New England Deaconess Hosp., Boston, MA 02215 USA

SOURCE:

FASEB Journal, (1996) Vol. 10, No. 6, pp. A1300.

Meeting Info.: Joint Meeting of the American Society for Biochemistry and Molecular Biology, the American Society for Investigative Pathology and the American Association of Immunologists New Orleans, Louisiana, USA June 2-6, 1996

ISSN: 0892-6638.

DOCUMENT TYPE:

Conference English

LANGUAGE:

General Biology - Symposia, Transactions and Proceedings of Conferences,

Congresses, Review Annuals 00520

Biochemical Studies - Proteins, Peptides and Amino Acids

Biochemical Studies - Carbohydrates Biophysics - Membrane Phenomena *10508

Metabolism - Carbohydrates *13004

Metabolism - Proteins, Peptides and Amino Acids *13012 Digestive System - Physiology and Biochemistry *14004

Immunology and Immunochemistry - Immunopathology, Tissue Immunology

*34508

Muridae *86375 BC

IT Major Concepts

> Digestive System (Ingestion and Assimilation); Immune System (Chemical Coordination and Homeostasis); Membranes (Cell Biology); Metabolism

IT Miscellaneous Descriptors

IMMUNOGLOBULIN G; MEETING ABSTRACT

ORGN Super Taxa

Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

mouse (Muridae)

ORGN Organism Superterms

animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;

rodents; vertebrates

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LAST RELOADED: Jun 20, 2003 (20030620/UP).

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	ENTRY	SESSION
FULL ESTIMATED COST	0.42	48.27
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	ENTRY	SESSION
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NEWS 5 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
                 now available on STN
NEWS 6 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 7 Sep 03 JAPIO has been reloaded and enhanced
NEWS 8 Sep 16 Experimental properties added to the REGISTRY file
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 10 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11 Oct 24 BEILSTEIN adds new search fields
NEWS 12 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13 Nov 18 DKILIT has been renamed APOLLIT
NEWS 14 Nov 25 More calculated properties added to REGISTRY
NEWS 15 Dec 04 CSA files on STN
NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17 Dec 17 TOXCENTER enhanced with additional content
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
                  ENERGY, INSPEC
NEWS 20 Feb 13 CANCERLIT is no longer being updated
NEWS 21 Feb 24 METADEX enhancements
NEWS 22 Feb 24 PCTGEN now available on STN
NEWS 23 Feb 24 TEMA now available on STN
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25 Feb 26 PCTFULL now contains images
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27 Mar 20 EVENTLINE will be removed from STN
NEWS 28 Mar 24
                 PATDPAFULL now available on STN
NEWS 29 Mar 24
                 Additional information for trade-named substances without
                 structures available in REGISTRY
NEWS 30 Apr 11
                 Display formats in DGENE enhanced
NEWS 31 Apr 14
                 MEDLINE Reload
NEWS 32 Apr 17
                 Polymer searching in REGISTRY enhanced
NEWS 33 Jun 13
                 Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34 Apr 21
                 New current-awareness alert (SDI) frequency in
                 WPIDS/WPINDEX/WPIX
NEWS 35 Apr 28
                 RDISCLOSURE now available on STN
NEWS 36 May 05
                 Pharmacokinetic information and systematic chemical names
                 added to PHAR
NEWS 37
         May 15 MEDLINE file segment of TOXCENTER reloaded
NEWS 38 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated
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NEWS 39 May 16 CHEMREACT will be removed from STN

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA

NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB

NEWS 43 Jun 06 PASCAL enhanced with additional data

NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available

NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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FILE 'SCISEARCH' ENTERED AT 15:43:35 ON 25 JUN 2003 COPYRIGHT 2003 THOMSON ISI

=> s IgG2

STN search for 09/256,156 15304 IGG2 L1=> s fusion protein 121147 FUSION PROTEIN => search Ch2 domain 1827 CH2 DOMAIN => s 11 and 12 and 13 779 L1 AND L2 AND L3 => s l1 and half-life 2806 L1 AND HALF-LIFE => l half-life L IS NOT A RECOGNIZED COMMAND The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>). => s half-life T.6 233321 HALF-LIFE => s 11 and 12 and 13 and 16 752 L1 AND L2 AND L3 AND L6 L7 => dup rem 17 PROCESSING COMPLETED FOR L7 752 DUP REM L7 (0 DUPLICATES REMOVED) => s not py>=2000 MISSING TERM BEFORE 'NOT' Search expressions cannot begin with operators. => 18 not py>=2000 L8 IS NOT A RECOGNIZED COMMAND The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>). => s 18 not py>=2000 3 FILES SEARCHED... 35 L8 NOT PY>=2000 => s 19 not py>=1999 L10 22 L9 NOT PY>=1999 => d ibib abs 1-22 L10ANSWER 1 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1998050431 PCTFULL ED 20020514 TITLE (ENGLISH): A METHOD FOR MAKING MULTISPECIFIC ANTIBODIES HAVING HETEROMULTIMERIC AND COMMON COMPONENTS TITLE (FRENCH): PROCEDE DE PREPARATION D'ANTICORPS MULTISPECIFIQUES PRESENTANT DES COMPOSANTS HETEROMULTIMERES INVENTOR(S): ARATHOON, Robert; CARTER, Paul, J.; MERCHANT, Anne, M.; PRESTA, Leonard, G.

PATENT ASSIGNEE(S): LANGUAGE OF PUBL.: GENENTECH, INC.

LANGUAGE OF PUBL. DOCUMENT TYPE: English Patent

PATENT INFORMATION:

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ

CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: PRIORITY INFO.:

WO 1998-US8762 A 19980430 US 1997-08/850,058 19970502 US 1997-60/050,661 19970624

ABEN The invention relates to a method of preparing heteromultimeric polypeptides such as bispecific

antibodies, bispecific immunoadhesins and antibody-immunoadhesin chimeras. The invention also

relates to the heteromultimers prepared using the method. Generally, the method provides a

multispecific antibody having a common light chain associated with each heteromeric polypeptide

having an antibody binding domain. Additionally the method further involves introducing into the

multispecific antibody a specific and complementary interaction at the interface of a first

polypeptide and the interface of a second polypeptide, so as to promote heteromultimer formation and

hinder homomultimer formation; and/or a free thiol-containing residue at the interface of a first

polypeptide and a corresponding free thiol-containing residue in the interface of a second

polypeptide, such that a non-naturally occurring disulfide bond is formed between the first and

second polypeptide. The method allows for the enhanced formation of the desired heteromultimer

relative to undesired heteromultimers and homomultimers.

ABFR

L'invention porte sur un procede de preparation de polypeptides heteromultimeres tels que des

anticorps bispecifiques, des immunoadhesines bispecifiques, et des chimeres

d'anticorps/immunoadhesines. Elle porte egalement sur des heteromultimeres prepares a l'aide dudit

procede. Ledit procede fournit normalement un anticorps multispecifique presentant une chaine legere

commune associee a chacun des polypeptides comportant un domaine de fixation d'un anticorps. Ledit

procede consiste en outre a provoquer dans l'anticorps multispecifique une interaction specifique et

complementaire au niveau de l'interface d'un premier polypeptide et de l'interface d'un deuxieme

polypeptide de maniere a promouvoir la formation d'un heteromultimere et a empecher celle d'un

homomultimere, et/ou a introduire un residu contenant un thiol libre, au niveau de l'interface d'un

premier polypeptide et un residu, contenant un thiol libre correspondant, au niveau de l'interface du deuxieme polypeptide, de maniere a former une liaison bisulfure n'apparaissant pas naturellement entre le premier et le deuxieme polypeptide. Ce procede permet d'accroitre la formation de l'heteromultimere desire par rapport a celle des heteromultimeres et homomultimeres non desires.

L10 ANSWER 2 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1998036072 PCTFULL ED 20020514

ACCESSION NUMBER: TITLE (ENGLISH):

NEURTURIN RECEPTOR

TITLE (FRENCH):

RECEPTEUR DE LA NEURTURINE

INVENTOR(S): KLEIN, Robert, D.;
ROSENTHAL, Arnon;
HYNES, Mary, A.

PATENT ASSIGNEE(S):

GENENTECH, INC.

LANGUAGE OF PUBL.: DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

DESIGNATED STATES

W :

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF

APPLICATION INFO.: PRIORITY INFO.:

CG CI CM GA GN ML MR NE SN TD TG
WO 1998-US3179 A 19980217
US 1997-08/802,805 19970609
US 1997-08/957,063 19971024

ABEN NTNRα NTNRα extracellular domain (ECD), NTNRα variants, chimeric NTNRα

(e.g., NTNRα immunoadhesion), and antibodies which bind thereto (including agonist and $% \left(1\right) =\left(1\right) +\left(1\right$

neutralizing antibodies) are disclosed. Various uses for these molecules are described, including

methods to modulate cell activity and survival by response to NTNRα-ligands, for example NTN, by providing NTNRα to the cell.

ABFR

L'invention concerne le recepteur de la neurturine α (NTNRα), le domaine

extracellulaire (ECD) du NTNRα, des variants du NTNRα, un NTNRα chimere (tel

qu'une immuno-adhesine du NTNRα) et des anticorps qui se fixent sur le NTNRα (notamment

des anticorps agonistes et neutralisants). Elle concerne egalement diverses utilisations de ces

reponse aux ligands du NTNRα, par exemple la neurturine, en fournissant a la cellule des NTNRα.

L10 ANSWER 3 OF 22 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1998006747 PCTFULL ED 20020514 TITLE (ENGLISH): USES FOR WNT POLYPEPTIDES UTILISATION DE POLYPEPTIDES WNT TITLE (FRENCH): INVENTOR(S): MATTHEWS, William; AUSTIN, Timothy, W. PATENT ASSIGNEE(S): GENENTECH, INC. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 9806747 A2 19980219 DESIGNATED STATES AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE W : ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1997-US13910 A 19970807 PRIORITY INFO.: US 1996-8/696,566 19960816 Uses for Wnt polypeptides in hematopoiesis are disclosed. In particular, in vitro and in vivo methods for enhancing proliferation, differentiation or maintenance of a hematopoietic stem/progenitor cell using a Wnt polypeptide, and optionally another cytokine, are described. ABFR On decrit des utilisations de polypeptides Wnt dans l'hematopoiese. On decrit notamment des procedes in vitro et in vivo destines a augmenter la proliferation, la differentiation ou la conservation d'une cellule souche/parente, et consistant a utiliser un polypeptide Wnt, ainsi que, le cas echeant, une autre cytokine. ANSWER 4 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1997040153 PCTFULL ED 20020514 TITLE (ENGLISH): AL-2 NEUROTROPHIC FACTOR TITLE (FRENCH): FACTEUR NEUROTROPHIQUE AL-2 CARAS, Ingrid, W. INVENTOR(S): PATENT ASSIGNEE(S): GENENTECH, INC. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE WO 9740153 A1 19971030 DESIGNATED STATES W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE

SN TD TG

WO 1997-US6345 A 19970417 US 1996-8/635,130 19960419

The present invention provides nucleic acids encoding AL-2 protein, as

Page 6

ABEN

APPLICATION INFO.: PRIORITY INFO.: well as AL-2 protein

produced by recombinant DNA methods. Such AL-2 protein and nucleic acid are useful in preparing

antibodies and antagonists and in diagnosing and treating various neuronal disorders and disorders

or conditions associated with angiogenesis.

ABFR L'invention concerne des acides nucleiques codant pour la proteine Al-2, ainsi que la proteine

AL-2 produite par des methodes faisant appel a de l'ADN de recombinaison. Ces proteines AL-2 et ces

acides nucleiques sont utiles pour preparer des anticorps et des antagonistes et pour diagnostiquer

et traiter differentes troubles neurologiques, ainsi que pour traiter les troubles et affections

pathologiques associes a l'angiogenese.

L10 ANSWER 5 OF 22

PCTFULL COPYRIGHT 2003 Univentio 1997034631 PCTFULL ED 20020514

ACCESSION NUMBER: TITLE (ENGLISH): TITLE (FRENCH):

IMMUNOGLOBIN-LIKE DOMAINS WITH INCREASED HALF LIVES DOMAINES ANALOGUES A L'IMMUNOGLOBULINE A DEMI-VIES

PROLONGEES

INVENTOR(S):

WARD, Elizabeth, Sally

PATENT ASSIGNEE(S):

BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM;

WARD, Elizabeth, Sally

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

English Patent

PATENT INFORMATION:

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML

MR NE SN TD TG

APPLICATION INFO.:

WO 1997-US3321 A 19970303 US 1996-60/013,563 19960318

PRIORITY INFO.: US 1996-60/013,563

ABEN Disclosed are recombinant vectors end

Disclosed are recombinant vectors encoding immunoglobulin-like domains and portions thereof,

such as antibody Fc-hinge fragments, subfragments and mutant domains with extended biological half

lives. Methods of producing large quantities of such domains, heterodimers, and fusion proteins

following expression by host cells are also reported. Described are antibody Fc and Fc-hinge

domains, which have the same in vivo stability as intact antibodies; and domains engineered to have

increased in vivo half lives. These DNA constructs and protein domains will be useful as templates

for in vitro mutagenesis and high resolution structural studies; for immunization and vaccination;

and for the production of recombinant antibodies or chimeric proteins with increased stability and

longevity for therapeutic and diagnostic uses.

ABFR Vecteurs recombinants codant des domaines analogues a l'immunoglobuline et des parties de ces

```
fragments de Fc-charniere
       (Fc-hinge) anticorpaux, a demi-vies biologiques prolongees. Des procedes
       de production en grandes
       quantites de tels domaines, heterodimeres et proteines fusionnees apres
       leur expression par des
       cellules hotes sont egalement decrits, ainsi que des domaines Fc et
       Fc-charniere anticorpaux, qui
       presentent la meme stabilite in vivo que les anticorps intacts; et des
       domaines genetiquement
       modifies de facon a presenter des demi-vies in vivo prolongees. Ces ADN
       de recombinaison et ces
       domaines proteiques seront utiles comme matrices pour la mutagenese in
       vitro et pour les etudes de
       structures de haute resolution; pour l'immunisation et la vaccination;
       ainsi que pour la production
       d'anticorps recombinants ou de proteines chimeriques a stabilite et
       longevite accrue destines a des
       usages therapeutiques et diagnostiques.
      ANSWER 6 OF 22
                        PCTFULL
                                   COPYRIGHT 2003 Univentio
ACCESSION NUMBER:
                        1997033912 PCTFULL ED 20020514
TITLE (ENGLISH):
                        USES OF GDNF AND GDNF RECEPTOR
TITLE (FRENCH):
                        UTILISATIONS DE GDNF ET DE RECEPTEURS DE GDNF
INVENTOR(S):
                        KLEIN, Robert, D.;
                        MOORE, Mark, W.;
                        ROSENTHAL, Arnon;
                        RYAN, Anne, M.
PATENT ASSIGNEE(S):
                        GENENTECH, INC.;
                        KLEIN, Robert, D.;
                        MOORE, Mark, W.;
                        ROSENTHAL, Arnon;
                        RYAN, Anne, M.
LANGUAGE OF PUBL.:
                        English
DOCUMENT TYPE:
                        Patent
PATENT INFORMATION:
                        NUMBER
                                         KIND
                                                    DATE
                        WO 9733912
                                            A2 19970918
DESIGNATED STATES
      W:
                       . AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
                        ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS
                        LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG
                        SI SK TJ TM TR TT UA UG US US UZ VN GH KE LS MW SD SZ
                        UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR
                        GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML
                        MR NE SN TD TG
APPLICATION INFO .:
                        WO 1997-US4363
                                             A 19970313
PRIORITY INFO.:
                        US 1996-8/615,902
                                                19960314
                        US 1996-8/618,236
                                                19960314
      GDNFR'alpha', GDNFR'alpha' extracellular domain (ECD), GDNFR'alpha'
      variants, chimeric GDNFRae
       (e.g., GDNFR'alpha' immunoadhesin), and antibodies which bind thereto
       (including agonist and
      neutralizing antibodies) are disclosed. Various uses for these molecules
      are described, including
      methods to modulate cell activity and survival by response to
```

GDNF, by providing GDNFR'alpha' to the cell. Also provided are methods

derniers, tels que des domaines mutants, des sous-fragments et des

GDNFR'alpha'-ligands, for example

ABEN

L10

for using GDNFR'alpha', GDNF, or agonists thereof, separately or in complex, to treat kidney diseases. ABFR L'invention concerne des GDNFR'alpha' (recepteurs des facteurs neurotrophiques derives de cellules gliales 'alpha'), le domaine extracellulaire (ECD) des GDFNR'alpha', des variants du GDNFR'alpha', le GDNFR'alpha' chimere (par ex. l'immunoadhesine de GDNFR'alpha') et des anticorps qui se lient a ces derniers (y compris, des anticorps agonistes et de neutralisation). L'invention traite aussi de differentes utilisations de ces molecules, y compris des procedes permettant de moduler l'activite et la survie des cellules par la reponse des GDNFR'alpha'-ligands, par exemple par le GDNF (facteur neurotrophique derive de cellules gliales), en alimentant la cellule en ${\tt GDNFR'alpha'}.$ L'invention decrit aussi des procedes pour utiliser des ${\tt GDNFR'alpha'},$ des ${\tt GDNF}$ ou des agonistes de ces derniers, separement ou en complexes, pour traiter les maladies renales. L10 ANSWER 7 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1997028267 PCTFULL ED 20020514 ANTIBODIES AND IMMUNOGLOBULIN FUSION PROTEINS HAVING TITLE (ENGLISH): MODIFIED EFFECTOR FUNCTIONS AND USES THEREFOR TITLE (FRENCH): ANTICORPS ET PROTEINES DE FUSION D'IMMUNOGLOBULINE PRESENTANT DES FONCTIONS D'EFFECTEUR MODIFIEES ET LEURS UTILISATIONS INVENTOR(S): GRAY, Gary, S.; CARSON, Jerry; JAVAHERIAN, Kashi; JELLIS, Cindy, L.; RENNERT, Paul, D.; SILVER, Sandra PATENT ASSIGNEE(S): REPLIGEN CORPORATION; GRAY, Gary, S.; CARSON, Jerry; JAVAHERIAN, Kashi; JELLIS, Cindy, L.; RENNERT, Paul, D.; SILVER, Sandra LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE -----WO 9728267 A1 19970807 DESIGNATED STATES W: AU CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE A 19970203 APPLICATION INFO.: WO 1997-US1698 PRIORITY INFO.: US 1996-8/595,590 19960202 ABEN CTLA4-immunoglobulin fusion proteins having modified immunoglobulin constant region-mediated effector functions, and nucleic acids encoding the fusion proteins, are described. The CTLA4-immunoqlobulin fusion proteins comprise two components: a first peptide having a CTLA4 activity and a second peptide comprising an immunoglobulin constant

region which is modified to reduce at least one constant region-mediated biological effector function relative to a CTLA4-IqG1 fusion protein. The nucleic acids of the invention can be integrated into various expression vectors, which in turn can direct the synthesis of the corresponding proteins in a variety of hosts, particularly eukaryotic cells. The CTLA4-immunoglobulin fusion proteins described herein can be administered to a subject to inhibit an interaction between a CTLA4 ligand (e.g., B7-1 and/or B7-2) on an antigen presenting cell and a receptor for the CTLA4 ligand (e.g., CD28 and/or CTLA4) on the surface of T cellsto thereby suppress an immune response in the subject, for example to inhibit transplantation rejection, graft versus host disease or autoimmune responses. Proteines de fusion de CTLA4-immunoglobuline presentant des fonctions d'effecteur par la region constante d'immunoglobuline modifiees, et acides nucleiques codant les proteines de fusion. Les proteines de fusion de CTLA4-immunoglobuline sont constituees de deux elements: un premier peptide presentant une activite CTLA4 et un deuxieme peptide comprenant une region constante d'immunoglobuline modifiee pour reduire au moins une fonction d'effecteur biologique par la region constante d'immunoglobuline, par rapport a une proteine de fusion CTLA4-IqG1. Les acides nucleiques decrits peuvent s'integrer dans differents vecteurs d'expression, lesquels peuvent a leur tour commander la synthese des proteines correspondantes dans differents hotes, en particulier les cellules eucaryotes. Les proteines de fusion de CTLA4-immunoglobuline decrites ici peuvent etre administrees a un sujet pour inhiber une interaction entre un liqand DTLA4 (par exemple, B7-1 et/ou B7-2) sur une cellule presentant un antigene et un recepteur pour le ligand CTLA4 (par exemple CD28 et/ou CTLA4) a la surface de cellules T pour supprimer ainsi une reponse immunitaire du sujet, par exemple pour inhiber le rejet de transplantation, les reaction de

L10 ANSWER 8 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1997020062 PCTFULL ED 20020514

TITLE (ENGLISH): IL-12 P40 SUBUNIT FUSION POLYPEPTIDES AND USES THEREOF TITLE (FRENCH): POLYPEPTIDES DE FUSION CONSTITUES DE LA SOUS-UNITE p40

D'IL-12 ET LEURS UTILISATIONS

INVENTOR(S): STEELE, Alan, W.; STROM, Terry, B.

greffon contre l'hote ou les reactions auto-immunes.

UNIVERSITY OF MASSACHUSETTS;

BETH ISRAEL HOSPITAL

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

PATENT ASSIGNEE(S):

NUMBER KIND DATE

ABFR

A1 19970605 WO 9720062 DESIGNATED STATES AU CA JP KR AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE APPLICATION INFO.: WO 1996-US19181 A 19961202 PRIORITY INFO.: US 1995-8/565,856 19951201 ABEN Disclosed are fusion polypeptides that include an IL-12 p40 subunit polypeptide covalently linked to an enzymatically inactive polypeptide. The fusion polypeptides have an increased in vivo half-life relative to the native IL-12 p40 subunit. The fusion polypeptides function as antagonists of the IL-12 receptor, and can be used, for example, as immunosuppressive agents (e.g., in treating autoimmune diseases or in inhibiting graft rejection) or to treat or prevent endotoxin-induced shock. ABFR L'invention concerne des polypeptides de fusion qui comportent un polypeptide correspondant a la sous-unite p40 d'IL-12 avec un polypeptide sans activite enzymatique. Les polypeptides de fusion ont une demi-vie in vivo plus importante que celle de la sous-unite p40 d'IL-12 native. Ces polypeptides de fusion agissent comme antagonistes des recepteurs d'IL-12 et peuvent etre utilises par exemple comme agents immunosuppresseurs (par exemple pour le traitement de maladies auto-immunes ou pour eviter le rejet de greffon) ou pour traiter ou empecher les chocs causes par des endotoxines. ANSWER 9 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1996027011 PCTFULL ED 20020514 A METHOD FOR MAKING HETEROMULTIMERIC POLYPEPTIDES TITLE (ENGLISH): TITLE (FRENCH): PROCEDE D'OBTENTION DE POLYPEPTIDES HETEROMULTIMERIQUES INVENTOR(S): CARTER, Paul, J.; PRESTA, Leonard, G.; RIDGWAY, John, B. PATENT ASSIGNEE(S): GENENTECH, INC. LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent PATENT INFORMATION: NUMBER KIND DATE _____ WO 9627011 Al 19960906 DESIGNATED STATES W : AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AZ BY KG KZ RU TJ TM AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG APPLICATION INFO.: WO 1996-US1598 A 19960205 PRIORITY INFO.: US 1995-8/399,106 19950301 The invention relates to a method of preparing heteromultimeric polypeptides such as bispecific antibodies, bispecific immunoadhesins and antibody-immunoadhesin chimeras. The invention also relates to the heteromultimers prepared using the method. Generally, the

method involves introducing

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a protuberance at the interface of a first polypeptide and a
       corresponding cavity in the interface
       of a second polypeptide, such that the protuberance can be positioned in
       the cavity so as to promote
       heteromultimer formation and hinder homomultimer formation.
       Protuberances are constructed by
       replacing small amino acid side chains from the interface of the first
       polypeptide with larger side
       chains (e.g. tyrosine or tryptophan). Compensatory cavities of identical
       or similar size to the
       protuberances are created in the interface of the second polypetide by
       replacing large amino acid
       side chains with smaller ones (e.q. alanine or threonine). The
       protuberance and cavity can be made
       by synthetic means such as altering the nucleic acid encoding the
       polypeptides or by peptide
       synthesis.
ABFR
       L'invention porte sur un procede de preparation de polypeptides
       heteromultimeriques tels que
       des anticorps et immunoadhesines bispecifiques et des chimeres
       d'anticorps-immunoadhesines. D'une
       maniere generale, le procede consiste a former une protuberance dans
       l'interface d'un premier
       polypeptide, et une cavite correspondante dans l'interface d'un deuxieme
       polypeptide de maniere a
       pouvoir positionner la protuberance dans la cavite afin de provoquer la
       formation d'un
       heteromultimere et empecher celle d'homomultimeres. Lesdites
       protuberances resultent du
       remplacement des petites chaines laterales d'acides amines de
       l'interface du premier polypeptide par
       des chaines laterales plus longues (par exemple de tyrosine ou de
       tryptophane). Des cavites
       compensatoires de taille identique ou similaire a celle des
       protuberances sont ainsi creees dans
       l'interfaces du deuxieme polypeptide en remplacant les longues chaines
       laterales d'acides amines par
       de plus courtes (par exemple des alanines et threonines). Les
       protuberances et cavites peuvent etre
       obtenues par synthese par exemple en modifiant l'acide nucleique codant
       pour les polypeptides, ou
      par la synthese de peptides.
L10
       ANSWER 10 OF 22
                         PCTFULL
                                   COPYRIGHT 2003 Univentio
ACCESSION NUMBER:
                        1996013518 PCTFULL ED 20020514
TITLE (ENGLISH):
                        AL-1 NEUROTROPHIC FACTOR, A LIGAND FOR AN EPH-RELATED
                        TYROSINE KINASE RECEPTOR
TITLE (FRENCH):
                        FACTEUR NEUROTROPHIQUE AL-1, UN LIGAND POUR LE
                        RECEPTEUR TYROSINE KINASE APPARENTE A EPH
INVENTOR (S):
                        CARAS, Ingrid, W.;
                        WINSLOW, John, W.
PATENT ASSIGNEE(S):
                        GENENTECH, INC.;
                        CARAS, Ingrid, W.;
                        WINSLOW, John, W.
LANGUAGE OF PUBL.:
                        English
DOCUMENT TYPE:
                        Patent
PATENT INFORMATION:
                        NUMBER
                                           KIND
                                                    DATE
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WO 9613518
                                           A1 19960509
DESIGNATED STATES
      W:
                       AL AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB
                       GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK
                       MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA
                       US UZ VN KE LS MW SD SZ UG AT BE CH DE DK ES FR GB GR
                       IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE
                       SN TD TG
APPLICATION INFO.:
                       WO 1995-US14016
                                            A 19951026
                       US 1994-8/330,128
PRIORITY INFO.:
                                               19941027
                       US 1995-8/486,449
                                               19950607
ABEN
       The present invention provides nucleic acids encoding AL-1 protein, as
       well as AL-1 protein
       produced by recombinant DNA methods. Such AL-1 protein is useful in
       preparing antibodies and
       antagonists and in diagnosing and treating various neuronal disorders
       and disorders or conditions
       associated with angiogenesis.
ABFR
      Cette invention presente des acides nucleiques codant une proteine de
       l'AL-1, ainsi qu'une
      proteine AL-1 produite par des methodes de genie genetique. Cette
      proteine AL-1 s'avere utile tant
      pour preparer des anticorps et des antagonistes que pour diagnostiquer
      et traiter divers troubles
      neuronaux ainsi que des troubles ou des etats pathologiques associes a
      l'angiogenese.
      ANSWER 11 OF 22 PCTFULL
                                  COPYRIGHT 2003 Univentio
ACCESSION NUMBER:
                       1996002645 PCTFULL ED 20020514
TITLE (ENGLISH):
                       HTK LIGAND
TITLE (FRENCH):
                      LIGAND DE HTK
INVENTOR(S):
                      BENNETT, Brian, D.;
                      MATTHEWS, William
                     GENENTECH, INC.
PATENT ASSIGNEE(S):
LANGUAGE OF PUBL.:
                      English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                      o NUMBER
                                KIND DATE
                       WO 9602645
                                           A2 19960201
DESIGNATED STATES
      W:
                       AU CA JP MX AT BE CH DE DK ES FR GB GR IE IT LU MC NL
                       PT SE
APPLICATION INFO.:
                       WO 1995-US8812
                                            A 19950714
PRIORITY INFO.:
                       US 1994-8/277,722
                                               19940720
      A novel hepatoma transmembrane kinase receptor ligand (Htk ligand) which
      binds to, and
      activates, the Htk receptor is disclosed. As examples, mouse and human
      Htk ligands have been
      identified in a variety of tissues using a soluble Htk-Fc fusion
      protein. The ligands have been
      cloned and sequenced. The invention also relates to nucleic acids
      encoding the ligand, methods for
      production and use of the ligand, and antibodies directed thereto.
ABFR
      L'invention se rapporte a un nouveau ligand du recepteur de la kinase
      transmembranaire d'un
      hepatome (ligand de Htk) qui se fixe au recepteur de Htk et l'active.
      Par exemple, des ligands de
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Htk de la souris et de l'homme ont ete identifies dans une variete de tissus a l'aide d'une proteine

de fusion de Htk-Fc soluble. Les ligands ont ete clones et seguences. L'invention se rapporte

egalement aux acides nucleiques codant le ligand, aux procedes de production et d'utilisation du

ligand et aux anticorps diriges contre celui-ci.

ANSWER 12 OF 22 PCTFULL COPYRIGHT 2003 Univentio L10

ACCESSION NUMBER: 1995025795 PCTFULL ED 20020514
TITLE (ENGLISH): HUMAN trk RECEPTORS AND NEUROTROPHIC FACTOR INHIBITORS
TITLE (FRENCH): RECEPTEURS DU trk HUMAIN ET INHIBITEURS D'AGENTS

NEUROTROPHIQUES

PRESTA, Leonard, G.; INVENTOR(S):

SHELTON, David, L.;

URFER, Roman

GENENTECH, INC.

PATENT ASSIGNEE(S): LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE ------WO 9525795 Al 19950928

DESIGNATED STATES

AU CA JP MX NZ AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE W:

APPLICATION INFO.: WO 1995-US3426 A 19950317 US 1994-8/215,139 19940318 US 1994-8/286,846 19940805 US 1994-8/359,705 19941220 PRIORITY INFO.:

The invention concerns human trkB and trkC receptors and their ABEN

functional derivatives. The

invention further concerns immunoadhesins comprising trk receptor

sequences fused to immunoglobulin

sequences.

ABFR La presente invention concerne des recepteurs du trkB et du trkC humains

et leurs derives

fonctionnels, ainsi que des immunoadhesines comprenant des sequences de recepteurs de trk humain

fusionnees avec des sequences d'immunoglobulines.

ANSWER 13 OF 22 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER:

1995021258 PCTFULL ED 20020514

TITLE (ENGLISH):

FUSION PROTEINS THAT INCLUDE ANTIBODY AND NONANTIBODY

PORTIONS

TITLE (FRENCH):

PROTEINES DE FUSION COMPRENANT DES PARTIES ANTICORPALES

ET NON ANTICORPALES

INVENTOR(S):

LAROCHELLE, William, J.; AARONSON, Stuart, A.;

DIRSCH, Olaf

PATENT ASSIGNEE(S):

UNITED STATES OF AMERICA, represented by THE SECRETARY,

DEPARTMENT OF HEALTH AND HUMAN SERVICES

LANGUAGE OF PUBL.:

English

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

KIND DATE WO 9521258 A1 19950810

DESIGNATED STATES

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w.
                        AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE
                        HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL
                        NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN KE MW SD
                        SZ AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF
                        BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:
                        WO 1995-US974
                                             A 19950201
PRIORITY INFO.:
                        US 1994-8/189,552
                                                19940201
       The high affinity which is characteristic of homodimers of IgG heavy
ABEN
       chains is achieved, along
       with favorable secretion and flexibility/adaptability properties, in a
       fusion protein that has a
       nonantibody portion, comprised of an effector domain, joined to the
       aminoterminal end of an
       IgG-derived sequence consisting of a hinge: CH2: CH3 segment which lacks a
       CH1 domain, with a
       heterologous signal peptide preferably provided upstream of the
       nonantibody portion. Chimeric
       molecules of this structure can be secreted readily in stable form by
       mammalian cells transfected
       with DNA encoding the molecule, and are amenable to rapid, efficient
       purification to homogeneity,
       for example, using protein A. These molecules are effective substitutes
       for monoclonal antibodies in
       contexts such as flow cytometry, immunohistochemistry,
       immunoprecipitation and ELISAs. A fusion
         protein as described also can be used in screening for
       agonists and antagonists to the cognate
       binding partner of the nonantibody portion of the fusion
       protein. Moreover, chimeric molecules in
       which the nonantibody portion contains a growth factor domain are
       internalized, essentially like the
       natural growth factor, in contrast to the situation that generally
       pertains with respect to
       antibodies which are directed to external receptor domains.
ABFR
       On obtient une affinite elevee caracteristique des homodimeres des
       chaines lourdes d'IgG, ainsi
       que des proprietes de secretion et de flexibilite/adaptabilite
       avantageuses, dans une proteine de
       fusion comprenant une partie non anticorpale, constituee d'un domaine
       effecteur, et liee a
       l'extremite N-terminal d'une sequence derivee d'IgG consistant en un
       segment charniere: CH2: CH3,
       exempt de domaine CH1, avec un peptide signal heterologue prevu, de
      preference, en amont de la
      partie non anticorpale. Des molecules chimeres presentant cette
       structure peuvent etre secretees
       facilement sous une forme stable par des cellules mammaliennes
       transfectees avec de l'ADN codant la
       molecule, et peuvent etre rendues homogene par purification rapide et
       efficace au moyen, par
       exemple, de la proteine A. Ces molecules sont des substituts efficaces
       d'anticorps monoclonaux dans
       le cadre de cytometries de flux, d'immunohistochimie,
      d'immunoprecipitations et d'essais ELISA. On
      peut egalement utiliser ladite proteine de fusion dans la detection
      d'agonistes et d'antagonistes du
      partenaire de liaison parent de la partie non anticorpale de ladite
      proteine de fusion. Des
      molecules chimeres dans lesquelles la partie non anticorpale contient un
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domaine de facteur de croissance sont, par ailleurs, interiorisees, essentiellement comme le facteur de croissance naturel, en contraste avec la situation dans laquelle les anticorps sont diriges contre des domaines de recepteur externe.

L10 ANSWER 14 OF 22 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1994003191 PCTFULL ED 20020513

TITLE (ENGLISH): NON-PEPTIDYL MOIETY-CONJUGATED CD4-GAMMA2 AND CD4-

IgG2 IMMUNOCONJUGATES, AND USES THEREOF
CH): IMMUNOCONJUGUES CD4-GAMMA2 ET CD4-IgG2 A

TITLE (FRENCH): IMMUNOCONJUGUES CD4-GAMMA2 ET CD4-IgG2 A
FRACTION CONJUGUEE NON PEPTIDYLE, ET LEURS UTILISATIONS

INVENTOR(S): ALLAWAY, Graham, P.;

MADDON, Paul, J.

PATENT ASSIGNEE(S): PROGENICS PHARMACEUTICALS, INC.;

ALLAWAY, Graham, P.; MADDON, Paul, J.

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL

PT SE

APPLICATION INFO.: WO 1993-US7422 A 19930806 PRIORITY INFO.: US 1992-7/927,931 19920807

ABEN This invention provides an immunoconjugate which comprises 1) a non-peptidyl toxin and 2) a

CD4-gamma2 chimeric heavy chain homodimer linked thereto. This invention also provides an

immunoconjugate which comprises 1) a gamma radiation-emitting radionuclide of low to moderate

cytotoxicity and 2) a ${\rm CD4}\operatorname{-gamma2}$ chimeric heavy chain homodimer linked thereto. This invention

further provides an immunoconjugate which comprises 1) a non-peptidyl toxin and 2) a heterotetramer

comprising two heavy chains and two light chains, both heavy chains being either a) IqG2 heavy

chains or b) chimeric CD4-IgG2 heavy chains, and both light chains being either a) kappa light

chains or b) chimeric CD4-kappa light chains. This invention further provides an immunoconjugate

which comprises 1) a gamma radiation-emitting radionuclide of low to moderate cytotoxicity and 2) a $\,$

heterotetramer comprising two heavy chains and two light chains, both heavy chains being either a)

IgG2 heavy chains or b) chimeric CD4-IgG2 heavy
chains, and both light chains being either a) kappa

light chains or b) chimeric CD4-kappa light chains. Finally, this invention provides methods of

using the immunoconjugates of the subject invention.

ABFR Cette invention concerne un immunoconjugue qui comprend 1) une toxine non peptidyle et 2) un

homodimere a chaine lourde chimerique CD4-gamma2 relie a ladite toxine. Cette invention concerne

egalement un immunoconjugue qui comprend 1) un radionuclide emettant un

rayonnement gamma d'une

chimerique CD4-gamma2 relie a

comprend 1) une toxine non

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peptidyle et 2) un heterotetramere comprenant deux chaines lourdes et
       deux chaines legeres, les deux
       chaines lourdes etant soit a) des chaines lourdes IgG2 soit b)
       des chaines lourdes chimeriques
       CD4-IgG2, et les deux chaines legeres etant soit a) des
       chaines legeres kappa soit b) des chaines
       legeres chimeriques CD4-kappa. Cette invention concerne egalement un
       immunoconjugue qui comprend 1)
       un radionuclide emettant un rayonnement gamma d'une cytotoxicite faible
       a moderee et 2) un
       heterotetramere comprenant deux chaines lourdes et deux chaines legeres,
       les deux chaines lourdes
       etant soit a) des chaines lourdes IgG2 soit b) des chaines
       lourdes chimeriques CD4-IgG2, et les deux
       chaines legeres etant soit a) des chaines legeres kappa soit b) des
       chaines legeres chimeriques
       CD4-kappa. Finalement, cette invention concerne des procedes
       d'utilisation des immunoconjugues de la
       presente invention.
      ANSWER 15 OF 22 PCTFULL
L10
                                  COPYRIGHT 2003 Univentio
ACCESSION NUMBER:
                       1993005072 PCTFULL ED 20020513
TITLE (ENGLISH):
                       DISEASE ASSOCIATED HUMAN AUTOANTIBODIES SPECIFIC FOR
                       HUMAN THYROID PEROXIDASE
TITLE (FRENCH):
                       AUTO-ANTICORPS HUMAINS ASSOCIES A UNE PATHOLOGIE
                       SPECIFIQUE A LA PEROXIDASE THYROIDIQUE HUMAINE
                       RAPOPORT, Basil
INVENTOR (S):
PATENT ASSIGNEE(S):
                       RAPOPORT, Basil
LANGUAGE OF PUBL.:
                       English
DOCUMENT TYPE:
                       Patent
PATENT INFORMATION:
                       NUMBER
                                KIND DATE
                       WO 9305072
                                           A1 19930318
DESIGNATED STATES
      W:
                       AU CA FI JP KR NO US AT BE CH DE DK ES FR GB GR IE IT
                       LU MC NL SE
APPLICATION INFO.:
                       WO 1992-US7381
                                            A 19920828
PRIORITY INFO.:
                       US 1991-7/750,579
                                               19910828
                       US 1992-PCT/US92/06283 19920730
      Disease associated human autoantibodies specific for human thyroid
ABEN
      peroxidase are disclosed.
      Novel organ-specific (TPO) human autoantibodies are disclosed which have
      been cloned, allowing
      definition of the autoantibody repertoire and the autoantigenic domains,
       encompassing a restricted
       immunodominant region on TPO recognized by patients with autoimmune
      thyroid disease. The novel
      compositions of the invention, their diagnostic and therapeutic
      applications, are, inter alia
      disclosed.
ABFR
      Auto-anticorps humains associes a une pathologie, specifiques a la
      peroxidase thyroidique
      humaine. L'invention concerne egalement de nouveaux anticorps humains
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cytotoxicite faible a moderee et 2) un homodimere a chaine lourde

celui-ci. Cette invention concerne egalement un immunoconjugue qui

(peroxidases thyroidiques)

specifiques a des organes, lesquels ont ete clones, permettant une definition d'auto-anticorps et

des domaines auto-antigeniques, recouvrant une region immuno-dominante limitee sur la peroxidase

thyroidique reconnue par des patients atteints d'une maladie a caractere auto-immunologique

affectant la thyroide. Les nouvelles compositions de l'invention, leurs applications diagnostiques

et therapeutiques sont, inter alia, decrites.

L10 ANSWER 16 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1992000985 PCTFULL ED 20020513

TITLE (ENGLISH): STREPTOMYCES VECTORS FOR PRODUCTION OF HETEROLOGOUS

PROTEINS

TITLE (FRENCH): VECTEURS DE STREPTOMYCES UTILISES DANS LA PRODUCTION DE

PROTEINES HETEROLOGUES

INVENTOR(S): BRAWNER, Mary, Ellen;

FORNWALD, James, Allan;

ARTHOS, James

PATENT ASSIGNEE(S): SMITHKLINE BEECHAM CORPORATION

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W :

AT AU BE CA CH DE DK ES FR GB GR IT JP KR LU NL SE

APPLICATION INFO.: WO 1991-US4663 A 19910701 PRIORITY INFO.: US 1990-551,584 19900711 US 1991-665,218 19910305

ABEN Nucleic acid sequences and DNA vectors useful for the production of CD4 chimeric proteins, as

well as other heterologous proteins, in Streptomyces are disclosed. The nucleic acid sequences of

the invention comprise the coding sequence for the signal peptide of the Streptomyces longisporus $% \left(1\right) =\left(1\right) +\left(1\right) +$

tyrosine inhibitor (LTI) gene operatively linked with a propeptide sequence consisting essentially

of an amino acid sequence coding for from one to about 6 amino acids, the sequence of said amino

acids selected to result in the formation in Streptomyces of a protein product having a homogeneous $% \left(1\right) =\left(1\right) +\left(1\right)$

amino terminus after processing to remove said signal peptide formed on the protein product during

synthesis of the protein product. In an alternative embodiment of the invention, the propeptide is $\frac{1}{2} \int_{\mathbb{R}^{n}} \frac{1}{2} \left(\frac{1}{2} \int_{\mathbb{R}^{n}} \frac{1$

omitted and the LTI signal peptide is operatively linked with a nucleic acid sequence coding for a

heterologous protein which has been modified to code for the sequence lys-ala- at the 3° end. The

invention also provides cells transformed with the nucleic acid sequences or vectors of the

invention, and methods of using the nucleic acid sequences and vectors of the invention to produce

heterologous proteins in Streptomyces.

ABFR Sequences d'acides nucleiques et vecteurs d'ADN utiles dans la production de proteines

chimeriques CD4, ainsi que d'autres proteines heterologues, dans des Streptomyces. Les sequences

d'acides nucleiques de l'invention comprennent la sequence codante pour le peptide signal du gene

inhibiteur de tyrosine Streptomyces Longisporus (ITL) fonctionnellement lie a une sequence

propeptidique composee essentiellement d'une sequence d'acides amines codant pour 1 a environ 6

acides amines, la sequence desdits acides amines choisie pour permettre la formation dans des

Streptomyces d'un produit proteique ayant une terminaison amino homogene apres traitement afin

d'eliminer ledit peptide signal forme dans le produit proteique pendant la synthese de ce dernier.

Dans un autre mode de realisation de l'invention, le propeptide est omis et le peptide signal ${\tt ITL}$

est fonctionnellement lie a une sequence d'acides nucleiques codant pour une proteine heterologue

ayant ete modifiee afin de coder pour la sequence lys-ala- a l'extremite 3'. L'invention concerne

egalement des cellules transformees a l'aide des sequences ou des vecteurs d'acides nucleiques de

l'invention, ainsi que des procedes d'utilisation des sequences et des vecteurs d'acides nucleiques

de l'invention afin de produire des proteines heterologues dans des Streptomyces.

L10 ANSWER 17 OF 22 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1991014438 PCTFULL ED 20020513

TITLE (ENGLISH): CHIMERIC ANTIBODIES WITH RECEPTOR BINDING LIGANDS IN

PLACE OF THEIR CONSTANT REGION

TITLE (FRENCH): ANTICORPS CHIMERIQUES UTILISANT DES LIGANDS DE LIAISON

DE RECEPTEURS A LA PLACE DE LEUR REGION CONSTANTE

INVENTOR(S): MORRISON, Sherie, L.;

SHIN, Seung-Uon

PATENT ASSIGNEE(S): THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW

YORK;

English

MORRISON, Sherie, L.;

SHIN, Seung-Uon

LANGUAGE OF PUBL.:

DOCUMENT TYPE: Patent

PATENT INFORMATION:

DESIGNATED STATES

W: AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL SE US

APPLICATION INFO.: WO 1991-US1844 A 19910320 PRIORITY INFO.: US 1990-496,409 19900320

ABEN The present invention provides a modified chimeric monoclonal antibody

comprising two molecules of each of two different polypeptides. The shorter polypeptides function

as the light chains of the antibody and the longer polypeptides function as the heavy chains of the

antibody. Moreover, the polypeptide which functions as a heavy chain has a variable region characteristic of a first mammal

and a constant region characteristic of a second mammal. Each polypeptide which functions as a light

ABFR

chain has a variable region characteristic of a mammal and a constant region characteristic of a mammal, wherein a receptor-binding ligand replaces at least a portion of the constant region of each of the polypeptides which function as the heavy chains of the antibody. Additionally, the present invention provides an immunologically reactive complex and a chimeric polypeptide. Finally, methods of using and producing the modified chimeric monoclonal antibodies, immunologically reactive complexes, and chimeric polypeptides are provided herein. Anticorps monoclonal chimerique modifie comprenant deux molecules de chacun de deux polypeptides differents. Les polypeptides courts font fonction de chaines legeres de l'anticorps et les polypeptides longs font fonction de chaines lourdes dudit anticorps. De plus, le polypeptide faisant fonction de chaines lourdes presente une caracteristique de region variable d'un premier mammifere ainsi qu'une caracteristique de region constante d'un second mammifere. Chaque polypeptide faisant fonction de chaine legere presente une caracteristique de region variable d'un mammifere ainsi qu'une caracteristique de region constante d'un mammifere, un ligand de liaison de recepteur remplacant au moins une partie de la region constante de chacun des polypeptides faisant fonction de chaines lourdes de l'anticorps. De plus, l'invention concerne un complexe immunologiquement reactif ainsi qu'un polypeptide chimerique. Enfin, l'invention concerne des

procedes d'emploi et de production des anticorps monoclonaux chimeriques modifies, des complexes immunologiquement reactifs et des polypeptides chimeriques.

ANSWER 18 OF 22 PCTFULL COPYRIGHT 2003 Univentio ACCESSION NUMBER: 1990001035 PCTFULL ED 20020513

TITLE (ENGLISH): CYTOTOXIC AGENT AGAINST SPECIFIC VIRUS INFECTION AGENT CYTOTOXIQUE POUR LE TRAITEMENT D'INFECTIONS TITLE (FRENCH):

VIRALES SPECIFIQUES BERGER, Edward, A.;

INVENTOR(S): MOSS, Bernard; FUERST, Thomas, R.;

MIZUKAMI, Tamio; PASTAN, Ira, H.;

FITZGERALD, David, J., P.;

CHAUDHARY, Vijay, K.

PATENT ASSIGNEE(S): THE UNITED STATES OF AMERICA, represented by THE

SECRETARY, UNITED STATES DEPARTMENT OF COMMERCE

LANGUAGE OF PUBL.: English DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER KIND DATE ______ WO 9001035 A1 19900208

DESIGNATED STATES

W: AT AU BE CH DE FR GB IT JP LU NL SE APPLICATION INFO.: WO 1989-US3267 A 19890724 PRIORITY INFO.: US 1988-223,270 19880723

US 1988-283,739 19881213 US 1989-334,304 19890427 US 1988-283,739

ABEN A chimeric gene directing the synthesis of hybrid recombinant

fusion protein in a suitable

expression vector has been constructed. The fusion

protein possesses the property of selective

cytotoxicity against specific virus-infected cells. A CD4(178)-PE40 hybrid fusion protein has been

made for selectively killing HIV-infected cells. A recombinant, soluble, truncated form of CD4

containing the active binding site for human immunodeficiency virus is provided. Novel hybrid

proteins containing human CD4 sequences linked to human immunoglobulin constant regions to inhibit

HIV infection are described.

ABFR Un gene chimerique dirige la synthese d'une proteine hybride recombinante obtenue par fusion

dans un vecteur approprie d'expression. La proteine obtenue par fusion presente une cytotoxicite

specifique a l'egarol de cellules infectees par des virus specifiques. Une proteine hybride obtenue

par fusion, CD4(178)-PE40, tue selectivement des cellules infectees par VIH. Une forme recombinante,

soluble et tronquee de CD4 contient le site actif de liaison du virus d'immunodeficience humaine. De

nouvelles proteines hybrides qui contiennent des sequences de CD4 humaine liees a des zones

constantes de l'immunoglobuline humaine inhibent l'infection par des VIH.

L10 ANSWER 19 OF 22 USPATFULL

ACCESSION NUMBER:

1998:159916 USPATFULL

TITLE:

INVENTOR(S):

Method of enhancing proliferation or differentiation of

hematopoietic stem cells using Wnt polypeptides Matthews, William, Woodside, CA, United States

Austin, Timothy W., Morgan Hill, CA, United States

PATENT ASSIGNEE(S):

Genentech, Inc., South San Francisco, CA, United States

(U.S. corporation)

NUMBER KIND DATE ---------PATENT INFORMATION: APPLICATION INFO.: US 5851984 US 5851984 19981222 US 1996-696566 19960816 (8)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: PRIMARY EXAMINER: Fitzgerald, David L. ASSISTANT EXAMINER: Basham, Daryl A. LEGAL REPRESENTATIVE: Svoboda, Craig G., Marschang, Diane L.

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 3923

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Uses for Wnt polypeptides in hematopoiesis are disclosed. In particular, in vitro and in vivo methods for enhancing proliferation or differentiation of a hematopoietic stem/progenitor cell using a Wnt polypeptide, and optionally another cytokine, are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 20 OF 22 USPATFULL

ACCESSION NUMBER: 1998:151090 USPATFULL

TITLE: Human TRK receptors and neurotrophic factor inhibitors INVENTOR(S): Presta, Leonard G., San Francisco, CA, United States

Shelton, David L., Pacifica, CA, United States

Urfer, Roman, Pacifica, CA, United States

Genentech, Inc., S. San Francisco, CA, United States PATENT ASSIGNEE(S):

(U.S. corporation)

NUMBER KIND DATE -----US 5844092 19981201 US 1994-359705 19941220 (8) PATENT INFORMATION:

APPLICATION INFO.:

Continuation-in-part of Ser. No. US 1994-286846, filed RELATED APPLN. INFO.: on 5 Aug 1994 which is a continuation-in-part of Ser. No. US 1994-215139, filed on 18 Mar 1994, now abandoned

DOCUMENT TYPE: Utility Granted FILE SEGMENT: PRIMARY EXAMINER: Huff, Sheela ASSISTANT EXAMINER: Reeves, Julie E.

LEGAL REPRESENTATIVE: Torchia, Timothy E., Johnston, Sean A.

NUMBER OF CLAIMS: 19 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 47 Drawing Figure(s); 28 Drawing Page(s)

LINE COUNT: 4265

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention concerns human trkB and trkC receptors and their functional derivatives. The invention further concerns immunoadhesins comprising trk receptor sequences fused to immunoglobulin sequences.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 21 OF 22 USPATFULL

ACCESSION NUMBER: 97:49532 USPATFULL

TITLE: Expression vectors encoding bispecific fusion proteins

and methods of producing biologically active bispecific

fusion proteins in a mammalian cell

Ledbetter, Jeffrey A., Seattle, WA, United States INVENTOR(S):

Gilliland, Lisa K., Seattle, WA, United States Hayden, Martha S., San Diego, CA, United States Linsley, Peter S., Seattle, WA, United States Bajorath, Jurgen, Everett, WA, United States Fell, H. Perry, Redmond, WA, United States

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, New York, NY, United

States (U.S. corporation)

NUMBER KIND DATE -----PATENT INFORMATION:

US 5637481 19970610 US 1993-121054 19930913 (8) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-13420, filed

on 1 Feb 1993, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: PRIMARY EXAMINER: Granted Guzo, David

LEGAL REPRESENTATIVE: Merchant, Gould, Smith, Edell Welter & Schmidt

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 23 Drawing Figure(s); 17 Drawing Page(s)

LINE COUNT: 2109

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides an expression vector encoding

monospecific or bispecific fusion protein. In one

embodiment the expression vector encodes a monospecific fusion

protein, which vector comprises a recombinant monospecific

single chain cassette comprising a DNA sequence encoding a first binding

domain capable of binding a cell surface antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 22 OF 22 USPATFULL

ACCESSION NUMBER: 97:36159 USPATFULL

TITLE:

Method for using Htk ligand

INVENTOR(S):

Bennett, Brian D., Pacifica, CA, United States

Matthews, William, Woodside, CA, United States

PATENT ASSIGNEE(S):

Genentech Inc., So. San Francisco, CA, United States

(U.S. corporation)

NUMBER KIND DATE -----PATENT INFORMATION:

APPLICATION INFO.:

US 5624899 19970429 US 1995-436044 19950505 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-277722, filed on 20 Jul

1994

DOCUMENT TYPE: FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: PRIMARY EXAMINER: Adams, Donald E. ASSISTANT EXAMINER: Gucker, Stephen

NUMBER OF CLAIMS:

LEGAL REPRESENTATIVE: Dreger, Walter H.

EXEMPLARY CLAIM:

1

NUMBER OF DRAWINGS:

12 Drawing Figure(s); 11 Drawing Page(s)

LINE COUNT:

3222

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel hepatoma transmembrane kinase receptor ligand (Htk ligand) which binds to, and activates, the Htk receptor is disclosed. As examples, mouse and human Htk ligands have been identified in a variety of tissues using a soluble Htk-Fc fusion protein. The ligands have been cloned and sequenced. The invention also relates to nucleic

acids encoding the ligand, methods for production and use of the ligand, and antibodies directed thereto.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FULL ESTIMATED COST

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